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16 May 1984

USSR REPORT
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Vol. 18, No. 2, March-April 1984

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YURIY ALEKSEYEVICH GAGARIN (FIFTIETH BIRTHDAY)

[Moscow KOSMICHESKAYA BIOLOGIYA I AVIAKOSMICHESKAYA MEDITSINA in Russian Vol 18, No 2, Mar-Apr 84 (signed to press 15 Feb 84) p 6

[Editorial]

[Text] On 9 March of this year, Yuriy Alekseyevich Gagarin, Hero of the Soviet Union, USSR Pilot-Cosmonaut and the first man to have flown in space, would have been 50 years old. The world will always revere the memory of Yu. A. Gagarin, the Columbus of space, who blazed the trail for mankind into the universe, starting a new era in the history of science, technology and culture.

It would be difficult to exaggerate the significance of the flight that Yu. A. Gagarin made on 12 April 1961. This is the logical outcome of the entire history of civilization, which is based on the achievements in numerous branches of science, technology and economics. This flight heralded an important historical landmark, since man's penetration into space opened up enormous opportunities for development of science, technology, culture and organization of production. In the close to 23 years that have elapsed since the flight of Yu. A. Gagarin, cosmonautics has made some giant steps, and thereby has made a perceptible contribution to the solutions of many extremely important scientific and national economic problems.

All this has the most direct bearing on space biology and medicine. Thanks to space research, we have acquired substantially deeper knowledge in such areas as gravity physiology, exobiology, radiobiology of corpuscular superhigh-energy radiation, physiology and symptomatology of the vestibular system and mechanisms of spatial orientation, physiology and pathology of fluid-electrolyte metabolism and hypokinesia. Space research has helped achieve some results in solving problems of habitability of confined quarters, individual and group life-support and safety systems, questions of professional medical and psychological screening, determination of criteria of the norm and pathology, dynamic medical monitoring and expertise. We should mention the considerable progress made in methodological armamentarium of our clinical medicine, refinement and miniaturization of diagnostic equipment with extensive use of computers.

One can judge the breadth of biomedical specialties that are presently working together with space biology and medicine from the spectrum of articles printed

in our journal, which has been published since 1967. Articles dealing with problems of space biology are also published in many other journals and collections, and in the form of monographs (they include, in particular, about 50 volumes in the "Problemy kosmicheskoy biologii" [Problems of Space Biology] series); they are discussed at international congresses and symposiums. The retrospective bibliography of worldwide literature dealing with biomedical and sociopsychological problems of spaceflights is evidence of the rapid growth in number of publications on this subject in the 15 years after 1961. A total of 4700 sources were recorded for the first 5 years, more than 8250 for the second and more than 10,000 for the third 5 years. Thus, space biology and medicine are perceptibly part of our life.

The flight of Yuriy Alekseyevich Gagarin proved to the whole world the high scientific-technological and cultural sophistication of our country, as well as the enormous advantages of the socialist system. The best features of Soviet man are concentrated in the image of Yu. A. Gagarin. He was a kind and charming person, lifeloving and optimistic, wise and resourceful, courageous and selfless, disciplined and loyal to his cause, the Soviet people and party, a true patriot of his homeland. In his latter years, Yu. A. Gagarin acquired the skill of a capable administrator and organizer. A colonel in the Soviet Army and communist, he directed all his efforts and thoughts to space exploration and its use exclusively for peaceful purposes, for the good of all mankind, in the interest of peace in the entire world.

All of the medical workers who prepared Yu. A. Gagarin for his historical spaceflight remember how easy and pleasant it was to work with him, how modest and industrious he was, and a remarkable friend.

Yuriy Alekseyevich Gagarin is always remembered by specialists in space biology and aerospace medicine in all their scientific research.

SURVEYS

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SOME ASPECTS OF DOSIMETRY IN STUDIES OF BIOLOGICAL EFFECTS OF NONIONIZING ELECTROMAGNETIC RADIATION

Moscow KOSMICHESKAYA BIOLOGIYA I AVIAKOSMICHESKAYA MEDITSINA In Russian Vol 18, No 2, Mar-Apr 84 (manuscript received 19 Oct 82) pp 7-22

[Article by V. N. Karpov, A. A. Galkin and B. I. Davydov]

[English abstract from source] In order to clarify mechanisms of biological reactions, it is very important to study the absorption and spatial distribution of the absorbed electromagnetic energy. The procedures and methods of calculating the electromagnetic energy absorption of biological specimens exposed to non-ionizing electromagnetic irradiation in a wide frequency range (0-300 GHz) are described. Also presented are formulas and plots to be used in calculating the specific absorption of the dose rate by biological specimens, with the inclusion of resonance absorption, polarization of the incident electromagnetic wave, presence of reflecting surfaces and grounding. The extrapolation of the average energy absorption from one animal species to another and to man is discussed, assuming that spatial and energy distributions are equivalent. The notion of the irradiation quality coefficient is introduced. The values of the coefficients are given as related to the irradiation frequency and polarization type. A mathematical relation is offered to determine the safety of a complex spectrum of electromagnetic irradiation. The relation takes into consideration different dimensionality of the parameters of the electromagnetic field in the low- and high-frequency ranges.

[Text] The development of radar, radio relay and space communication, television and radionavigation, radioastronomy and radiospectroscopy, nuclear physics and medicine, and many other branches of science and technology is inseparably linked with use of electromagnetic radiation (EMR), in particular, in the range of superhigh frequencies. The energy of EMR sources, particularly in areas related to aviation and space exploration, has increased by 10-30 times in a decade. The intensity of electromagnetic fields (EMF) in the immediate vicinity of high-power emitting installations could exceed by many times, not only the natural electromagnetic background (NMB), but the standards set for it. All this puts a number of tasks to researchers, involving the study of biophysics of EMF interaction with biological systems and dosimetric evaluation of absorbed energy [4-6].

EMF interaction with matter, and in particular with a biological object, leads to absorption of some of the field energy by this matter. The observed biological effects of such interaction are the result of EMF energy absorption by atoms, molecules, cells, tissues, organs and the body as a whole. Any tested effect, the appearance of which is ascribed to EMR, is the consequence of absorption by the tested object of part of the radiation energy. According to the principle of Grotthaus, only the part of radiation energy absorbed by a substance can elicit changes in it; reflected or transmitted energy has no effect.

Strict use of the term, dosimetry, in radiobiology implies primarily an instrument or measuring method of evaluating absorbed dose rate or radiation dose in different media. However, the distinctions of EMR interaction with biological systems in the range of nonionizing radiations compels researchers to examine it in a broader aspect, in particular with use of methods of determining the absorbed energy in biological objects. Moreover, the desire to adequately conceive of the physical aspects of interaction of radiation at different frequencies with biological systems has resulted in having virtually all scientific work of the last decade dealing with principles of dosimetry of nonionizing EMR use exclusively some mathematical method of evaluating dosimetric parameters. In the case of using instruments for this purpose, the need to take into consideration distinctions of radiation interaction with biological objects such as polarization, resonance absorption and distribution of absorbed energy in depth raises major difficulties. To date, sensors of absorbed electromagnetic energy that could be implanted and would depend on spatial direction have not been developed. It is necessary to note that many specialists have a negative attitude toward developing such gages due to the exceptional difficulty of building them. Moreover, they believe that their use would yield a rather limited amount of useful information. For this reason, mathematical methods of evaluating EMR absorption in biological systems have gained a firm foothold in EMF dosimetry.

The overall amount of absorbed energy and its distribution in a biological object are a complex function of electrical properties of its tissues, overall geometric dimensions and irradiation conditions [7-9]. The link between EMF energy hitting a unit of body area per unit time and occurring distribution of specific absorption is determined by numerous parameters. For this reason, dosimetric studies of spatial distributions of specific absorbed power (SAP) are needed, not only for quantitative description of effects of EMF interaction with solids, but to elaborate the bases for subsequent extrapolation of biological effects from animals to man. It is validly noted, in particular in [10-11], that dosimetry of nonionizing EMR, which is developing intensively in recent years, is a discipline that still does not have an established terminology. Table 1 lists the physical characteristics of EMR interaction with biological objects and their designations.

The distribution of EMF in dielectrics of any form is described, in the general case, by Maxwell's equations [12-13]. The electrical properties and geometric dimensions permit, in theory, calculation of coefficients of reflection on the interfaces of different tissues and air, as well as magnitude of endogenous fields and induced current as a function of characteristics of external EMF.

Table 1. Physical characteristics of EMR interaction with biological specimens and their designations

| Phenomenon | Terms and abbreviations used in the literature | Terms and abbreviations used here | Letter designation | Unit of measurement |
|--|---|---|---|---------------------|
| Energy transmitted from EMR source through normally situated solitary area per unit time in zone of formed flat wave | Energy flux density (EFD), power flux density (PFD), power density (PD), intensity, energy flux, power flux, incident power flux, Umov-Pointing vector [In English] power density, intensity, magnitude of Pointing vector, exposure rate, flux energy density, etc. | Intensity, energy flux density, energetic illumination (in SI units) | I | W/m^2 |
| Part of EMF energy absorbed per unit body volume or mass per unit time | Specific absorption (SR), absorbed energy, absorbed power, microwave absorption rate, absorbed power density (APD), specific absorbed power, specific power [In English] absorbed power density, absorbed dose rate, specific absorbed rate (SAR), specific absorbed power (SAP), etc. | Specific absorbed power (SAP) per unit volume per unit mass SAP averaged for body volume (V) SAP averaged for body mass (M) | P P_v P_m $P_{av} = P_a/V$ $P_{am} = P_a/M$ | W/m^3 W/kg |
| Part of EMF energy absorbed by entire body per unit time | Absorbed energy, total absorbed power, integral dose [In English] absorbed power density, total absorbed power, integral dose rate, etc. | Total absorption of power (TAP) | $P_a = \int_V P_v dV = \int_M P_m dM$ | W |
| Part of EMF energy absorbed per unit volume or mass over a time interval | Rate of microwave absorption, dosage, total absorption, absorbed energy, radiation work. [In English] energy work, dose radiation, etc. | Specific energy absorption (SAP), dose | $D = \int_0^t P(t) dt$ | J/kg |

When the object is of limited size, the internal EMF will be a complex function of shape and dimensions of this object, as well as its orientation in relation to field vectors. At low frequencies, time of relaxation of free and bound charges within biological tissue is short, as compared to period of oscillations of applied field (ϵ^* is high), which leads to considerably greater field reduction within the biological specimen than in the short-wave radiation range.

The nature of biophysical interaction of specimens with EMF and the induced biological effects have attracted the attention of researchers for many years [14-18]. At the present time, it is impossible to give even a short list of researchers working in this area and of the effects they demonstrated. For dosimetry purposes, the work dealing with theoretical and experimental simulation of absorption processes in tissue-equivalent phantoms of different configurations were found to be the most useful [19-21]. Experimental studies to assess the influence of polarization, frequency and conditions of irradiation on the process of EMF energy absorption by a biological object in free space have become fruitful [20-23]. Several researchers determined the SAP averaged for a body according to temperature elevation (ΔT) in human models of different length [20, 21].

$$P_{am} = 4186 \cdot c \cdot \Delta T / t, \text{ W/kg} \quad (1)$$

where c is heat capacity of tissue (in cal/g \cdot °C) and t is exposure time (in s). Figure 1 illustrates SAP averaged for body mass for human models exposed to flat electromagnetic waves (EMW) in free space at field intensity of 1 mW/cm² for models with different orientation in the field of polarized radiation.

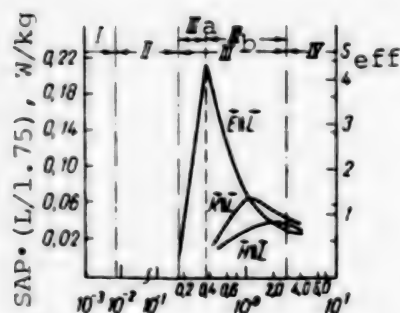


Figure 1.
SAP averaged for body mass as a resonance function of L/λ ratio for models in different positions in polarized free EMF with intensity of 1 mW/cm²

Vector \vec{L} coincides with the segment that connects the farthest points of the object. Extrapolation of the values to a model of arbitrary length L can be made by using a factor obtained from the ratio of model length to average human height (1.75 m) [21, 24, 25]. Use of other arbitrary intensities alters proportionately the scale divisions for SAP. For example, at an intensity of 10 mW/cm², the scale factor increases by 10 times.

As is the case for any physical interaction, the section of interaction or (for EMW) relative effective absorption section (S_{eff}), defined as the ratio of total dose rate absorbed by body to total power falling on its cross section in a plane that is perpendicular to the EMR front is demonstrative of its characteristics (see Figure 1) [26].

Experimental and theoretical studies [8-9, 23-27] made it possible to demonstrate energy absorption by models of biological objects specific for EMF, which is manifested by significant increase in absorption section for limited frequency

ranges. Studies of animals [17, 20, 28-30] confirmed the existence of a dependence of absorption intensity on orientation of vectors of electric and magnetic intensities, \vec{E} and \vec{H} respectively, of fields, or vector of direction of distribution \vec{k} ($\vec{k} = [\vec{E} \times \vec{H}]$ is the Umov-Poynting vector) in relation to vector \vec{L} . Most theoretically predicted results are referable to geometrically regular solids. And, although they are rather rough approximations of existing biological objects, consideration of these simple models is useful to gaining understanding of the basic patterns determining processes of dissemination and absorption of energy in animals and man.

We should mention the significant differences in processes of induction of endogenous fields of the electric and magnetic components of incident radiation, which leads to substantial differences in specific absorption of electric (P_E) and magnetic (P_H) parts of SAP. For example, for spherical models at low frequencies, the endogenous field (E_{en}) is $3/\epsilon^*$ times lower than the exogenous one [12-13], there being uniform SAP over the entire volume, regardless of the sphere's radius [8-9, 12-13]. Under the same conditions, the magnetic component of the waves generates SAP that increases proportionately to the square of the distance from the plane of H polarization. The solution of Maxwell equations for a sphere in the field of a flat EMW under conditions of quasistatic [8-9, 12-13] approximation enables us to write down an expression that is suitable for calculating mean SAP both in the zone of the formed wave and in the near zone, i.e., regardless of ratio between \vec{E} and \vec{H} , including the cases of purely electric or magnetic fields:

$$P_{av} = P_E + P_H = 4.5 \cdot \frac{\sigma \cdot E_0^2}{\epsilon^2 (1 + \lg^2 \delta)} + 0.28 \cdot 10^6 \cdot \sigma \cdot \left(\frac{L}{2\lambda} \right)^2 \cdot H_0^2, \text{ W/m}^3. \quad (2)$$

All of the symbols refer to the above-mentioned parameters in SI units. This equation enables us to stress the influence of dimensions of biological objects on processes of absorption of the magnetic component of mean SAP. Thus, the averaged SAP in a spherical human model is more than 300 times higher (for the magnetic component) than for mice with the same intensities of incident waves [8-9].

There are good explanations of the mechanisms of occurrence of peaks of resonance absorption (see Figure 1) based on antenna theory and continuity requirements for the tangential component of EMF in several works [23, 26]. However, it should be stressed that, in the case of \vec{E} polarization ($\vec{E} \parallel \vec{L}$), optimum conditions are created also for absorption of energy transported by the \vec{H} component of the field, since in this case the body dimension perpendicular to the plane of H polarization is at a maximum.

Analysis of Figure 1 and Table 2 will yield a general idea about dosimetric principles and methods used to evaluate EMF energy absorption by biological objects when they are exposed to flat waves in free space.

Table 2. Ranges, formulas and figures for determination of SAP as a function of L/λ ratio and irradiation conditions (see Figure 1)

| Object | L, m | M, kg | Range | | | | | |
|-------------------------------------|--------------------|-------|--|--|---|---|-----------|--|
| | | | I | II | IIIa | Resonance conditions | | IIIb |
| | | | $L/\lambda \leq 0.006$ f_{li} , MHz | $L/\lambda \leq 0.1 + 0.2$ f_{li} , MHz | $L/\lambda \leq 0.36$ f_{li} , MHz | $L/\lambda = 0.36 + 0.4$ f_{res} , MHz | S_{res} | $L/\lambda \leq 2.6$ f_{li} , MHz |
| Nan | 1.75 | 70 | ! | 30 | 67 | 68 | 4.2 | 0.46 |
| Monkey | 0.4 | 3.5 | ! | 150 | 290 | 297 | 3.2 | 1.5 |
| Dog | 1.12 | 15.0 | ! | 60 | 100 | 107 | 7.3 | 1.25 |
| Rabbit | 0.4 | 1.0 | ! | 150 | 290 | 296 | 6.1 | 2.9 |
| Rat | 0.15 | 0.2 | ! | 300 | 790 | 792 | 3.1 | 3.9 |
| Mouse | 0.0536 | 0.02 | ! | 809 | 2200 | 2216 | 2.1 | 7.5 |
| Formulas & figures for calculations | in free space | | (4),(5),(6)* | (7),(8) Fig 2 (a*,b*,c*) | (12),(13),** (16) Fig 4 | (9), (10),(11),(16) Fig 3a*, 4 | | (14)*,(15),**,(16) Fig 3a*, 4 |
| | contact with earth | | (3)* | 3b* and 3c* | | | | |
| | | | | | | | | — |

Key: *) only for human models

**) only for laboratory animal models

L) maximum size of object

M) mean mass of biological object

λ) radiation wavelength

f_{res}) resonance SAP frequency

f_{li}) limit frequency of range

S_{res}) effective interaction section with resonance

Development of theoretical and empirical procedures of EMR dosimetry calculations occurred through evolution from simple models to models close to living bodies in shape and structure. In early studies, calculation was made of energy absorbed in flat [19, 22, 32, 33], spherical [8-9, 31, 34-41] and cylindrical [42-45] models of man and animals. More recent models consisting of cubic cells [46-49] and spheroids of revolution [26, 33, 50] led to ellipsoid models of more complex appearance [34, 53-56]. However, each of the above-mentioned methods leads to an adequate evaluation of absorbed energy only within a limited range of frequencies. At the same time, their integrated consideration yields a conception of electromagnetic dosimetry that is acceptable at the present time [28, 57, 58]. We should stress once more that the most general method of calculating absorbed energy in any model is to find strict solutions to Maxwell equations [12-13, 49]. And, although these equations are rather complicated, a skillful choice of models and solution methods makes it possible to obtain the needed information about absorption and even distribution of absorbed energy in bodies of complex structure and configuration.

Use of computers for numerical solutions to Maxwell equations in the frequency range to about 600 MHz yields data about the distribution of local SAP [34, 46-48, 52, 57, 58]. However, it is a difficult task to construct unitized models for each specific case, with consideration of electrical properties of the cell and recording of boundary conditions. Moreover, a change in position or configuration of the body makes it necessary to rewrite the boundary conditions. With decrease in wavelength, there is reduction of intrinsic spatial variations of a field which, in turn, leads to an increase in number of equations in the system, the total number of which is limited by the computer's memory. At the same time, numerical solution methods (or unitized modeling), which consist of direct solution of Maxwell equations, are the direct and only means of obtaining reliable information about distribution of specific absorption of power in biological systems.

For practical estimates of SAP of average volume as a function of frequency ranges for models of man and laboratory animals, one can use several methods that take into consideration dimensions, configuration and irradiation conditions. Significant relative dielectric permeability of tissue and its low conductivity lead to substantial attenuation of applied intensities in the body during interaction of biological systems with stationary electric and infralow-frequency EMF (see Figure 1, interval 1).

The shielding superficial density of induced charges depends primarily on shape of a body, its dimensions, location and orientation in relation to earth. The lines of force of the external field are perpendicular to the surface of the object. Field intensity is different on the body surface. For example, during interaction with vertically oriented electric fields at commercial frequencies, the top part of the head of a person standing on earth intensifies the field by 18 times, his face does so by 20 times, occiput by 15 times, while the arms increase it by 8 times [59]. Overall induced current (i_0) in a person with height L (m) standing on earth, in a field with intensity E (V), can be found using the following equation [7, 29]:

$$i_0 = 5.4 \cdot 10^3 \cdot L^2 \cdot E, \text{ A} \quad (3)$$

In order to determine density of current passing through the cross section of the neck, chest, thighs, upper legs, each ankle and upper arm, it is necessary to multiply the obtained value by the following factors: 0.30, 0.75, 0.85, 0.93, 0.50 and 0.14, and divide by the area of the corresponding sections. Total current passing through a grounded person under these conditions consists of superficial currents and currents attributable to intensity of the endogenous field. According to [7], density of currents oriented normally to the body surface is determined as follows:

$$j = 2\pi \cdot f \cdot \epsilon_0 \cdot E_n, \text{ A/cm}^2 \quad (4)$$

where E_n is electric field intensity on body surface, which depends on slope; $\epsilon_0 = 8.85 \cdot 10^{-12}$ (in F/m) is dielectric constant. For example, for a man 1.7 [m] tall standing on earth, overall current in a field of 10 kV will constitute $1.6 \cdot 10^{-7}$ A according to equation (3). Current density through the neck, with cross section of 85 cm², will be $5.5 \cdot 10^{-10}$ (in A/cm²). Density of current oriented perpendicularly to the top of the head is found using equation (4) and constitutes $0.6 \cdot 10^{-10}$ A/cm².

With exposure to radiation in free space at frequencies up to approximately 1 MHz, the dimensions of animal and human bodies are small in comparison to wavelength and there are minimal dielectric processes in tissues. For this reason, the human or animal body can be considered a homogeneous conducting ellipsoid [26, 60]. Density of currents induced by the electric (\vec{E}) and magnetic (\vec{H}) components of the field, respectively, can be defined using the following equations [7, 17, 76]:

$$\begin{aligned} j_E &= 1.3 \cdot 10^{-9} \cdot f \cdot E, \text{ A/m}^2 \\ j_H &= 1.3 \cdot 10^{-7} \cdot f \cdot H, \text{ A/m}^2 \end{aligned} \quad (5)$$

Considering that heating is proportionate to the square of total (through cross section) current and tissue resistance for a human body of average height and mass and using the spheroid model, we can write down the equation for heat emitted in the body as follows [61]:

$$\begin{aligned} Q_E &= 2 \cdot 10^{-21} \cdot \rho \cdot f^2 \cdot E^2, \text{ cal/min} \\ Q_H &= 2 \cdot 10^{-17} \cdot \rho \cdot f^2 \cdot H^2, \text{ cal/min} \end{aligned} \quad (6)$$

where f is frequency of electromagnetic oscillations (EMO) (in Hz); $\rho = \frac{1}{\sigma}$ is average resistance of human tissues (in $\Omega \cdot \text{m}$; for example, at a frequency of 50 Hz $\rho \approx 9 \Omega \cdot \text{m}$). Overall heat emission is $Q = Q_E + Q_H$.

At the present level of development of dosimetry of nonionizing radiation, the second range has been worked on the most fruitfully; for man it is the interval approximately from 1 to 30 MHz (see Figure 1). It was possible to construct ellipsoid models of laboratory animals and man, as well as to obtain the ratios for calculation of SAP distributions within ellipsoids and to study the polarization phenomenon in this range by satisfying conditions of quasistatic

approximation ($\lambda \gg 10 L$), as well as inequality $\epsilon_2 \gg \epsilon_1$, where ϵ_1 and ϵ_2 are true and imaginary parts of combined dielectric permeability. In addition, one can also use numerical methods of solving the Maxwell equations, which permits comparison of estimates made by these methods.

If we were to place the start of the coordinates in the center of the ellipsoid, the coordinates at any point within its volume will satisfy the inequality:

$$x^2/a^2 + y^2/b^2 + z^2/c^2 \leq 1,$$

where a , b and c are axes of the ellipsoid. In the terminology of the authors of [51], hereafter we shall assume that $a > b > c$. Mean specific absorption of power within the ellipsoid will be:

$$P_v(x, y, z) = \frac{1}{2} \cdot \sigma \cdot |\vec{E}|^2, \text{ W/m}^3$$

and the spatially averaged absorption of power will be expressed by the following integral [51]:

$$P_{av} = \frac{1}{V} \int_{z=-c}^c \int_{x=-a}^a \int_{y=-f(x,z)}^{f(x,z)} P_v(x, y, z) dx dy dz,$$

where

$$f(x, z) = b \left(1 - \frac{x^2}{a^2} - \frac{z^2}{c^2} \right)^{1/2} \text{ and } V = 4\pi abc/3.$$

In free space, the ellipsoid model may present six different orientations in relation to vectors of dissemination and planes of polarization: EKH, EHK, KEH, KHE, HEK, HKE. Proper reading of such polarizations consists of the following: the vector parallel to the largest axis is read as the first and the one that is parallel to the smallest axis, the last. The solution for zero and first-order smallness of Maxwell equations for a flat wave falling on a tissue-equivalent ellipsoid when it is oriented in different directions in relation to polarization planes can be written down in the following form [51]:

$$\begin{aligned} EKH & \begin{cases} P_v(x, y, z) = D [(A_x + C_z y)^2 + B_z x^2] \\ P_{av} = D (A_x^2 - a^2 B_z/5) \end{cases} \\ EHK & \begin{cases} P_v(x, y, z) = D [(A_x + B_y z)^2 + C_y^2 x^2] \\ P_{av} = D (A_x^2 + C^2 B_y/5) \end{cases} \\ KEH & \begin{cases} P_v(x, y, z) = D [(A_y + B_z x)^2 + C_z y^2] \\ P_{av} = D (A_y^2 - a^2 B_z/5) \end{cases} \\ KHE & \begin{cases} P_v(x, y, z) = D [(A_z + C_y x)^2 + B_y^2 z^2] \\ P_{av} = D (A_z^2 + C^2 B_y/5) \end{cases} \\ HEK & \begin{cases} P_v(x, y, z) = D [(A_y + C_x z)^2 + B_x y^2] \\ P_{av} = D (A_y^2 + b^2 B_x/5) \end{cases} \\ HEK & \begin{cases} P_v(x, y, z) = D [(A_y + C_x z)^2 + B_x y^2] \\ P_{av} = D (A_y^2 + b^2 B_x/5) \end{cases} \end{aligned} \quad (7)$$

$$HKE \begin{cases} P_v(x, y, z) = D [(A_z + B_x y)^2 + C_x^2 z^2] \\ P_{av} = D (A_z^2 + b^2 B_x/5), \end{cases}$$

$$\text{where } D = \frac{1}{2} \sigma \omega^2 \mu_0 \epsilon_0 E^2; A_x = -1/\sigma \eta_0 A_1;$$

$$A_y = -1/\sigma \eta_0 A_2; A_z = -1/\sigma \eta_0 A_3;$$

$$A_1 = abc [F(\varphi, k)] / (a^2 - b^2) \cdot \sqrt{a^2 - c^2};$$

$$A_3 = abc \left[\frac{b}{a} \operatorname{tg} \varphi - E(\varphi, k) / (b^2 - c^2) \times \right. \\ \left. \times \sqrt{a^2 - c^2}; \right.$$

$$A_2 = abc \sqrt{a^2 - c^2} [E(\varphi, k) - \\ - (b^2 - c^2) F(\varphi, k) / (a^2 - c^2) - \\ - (ak^2 \sin \varphi \cos \varphi) / b^2] / (a^2 - b^2) (b^2 - c^2); \\ k = \sqrt{(a^2 - b^2) / (a^2 - c^2)};$$

$$\varphi = \arcsin \sqrt{(a^2 - c^2) / a^2}; B_x = c^2 / (b^2 + c^2);$$

$$B_y = a^2 / (a^2 + c^2);$$

$$B_z = -b^2 / (a^2 + b^2); C_x = -b^2 / (b^2 + c^2);$$

$$C_y = -c^2 / (a^2 - c^2); C_z = a^2 / (a^2 + b^2);$$

$$F(\varphi, k) = \int_0^{\varphi} (1 - k^2 \sin^2 \theta)^{-1/2} d\theta;$$

$$E(\varphi, k) = \int_0^{\varphi} (1 - k^2 \sin^2 \theta)^{1/2} d\theta,$$

where $F(\varphi, k)$ and $E(\varphi, k)$ are incomplete elliptical integrals, the values of which are tabulated. With all the apparent unwieldiness of the above equations, computation of distributions of SAP and SAP averaged for ellipsoid volume is rather simple and amounts to several successive operations for each polarization. The process is made easier if one takes into consideration that, from the adopted relationship $a < b < c$ one has $A_1 > A_2 > A_3$ and the sum $A_1 + A_2 + A_3 = 1$.

It is useful to analyze the SAP ellipsoid averaged for total mass as a function of EMF frequency to assess the influence of location of polarization planes in relation to the ellipsoid axes (Figure 2) [52]. There is obvious prevalence of energy absorption with the side of the model exposed to radiation and vector \vec{E} oriented parallel to the maximum axis of the ellipsoid. The form of exposure that is second in significance is in the direction of the chest or back with analogous \vec{E} orientation. The distribution of radiation along the maximum dimensions of the body with vector \vec{E} oriented from arm to arm is also significant. Other types of polarization constitute only a small part of the conditions of maximum absorption. Consequently, it can be said that the position of the body with the side toward radiation, with coincidence of maximum axis and vector of magnetic intensity, is the safest.

In order to facilitate estimation of averaged SAP for body mass, Figure 2b illustrates SAP as a function of EMO frequency with different polarizations. The plots in Figure 2a and 2b were made for human and laboratory animals, data about which are listed in Table 3. Figure 2c provides useful information

about the averaged SAP in ellipsoid models of different types of humans with EKH polarization and exposure in free space to flat EMW with intensity of 1 mW/cm^2 [52]. Data about other intensity levels can be obtained by simple linear extrapolation of the obtained SAP values. However, these functions only permit estimation of SAP averaged for volume within the frequency range under consideration. Information about the distribution of SAP over the volume of the ellipsoid as a function of coordinates of the point of interest and irradiation conditions can, if necessary, be obtained directly from equations (7).

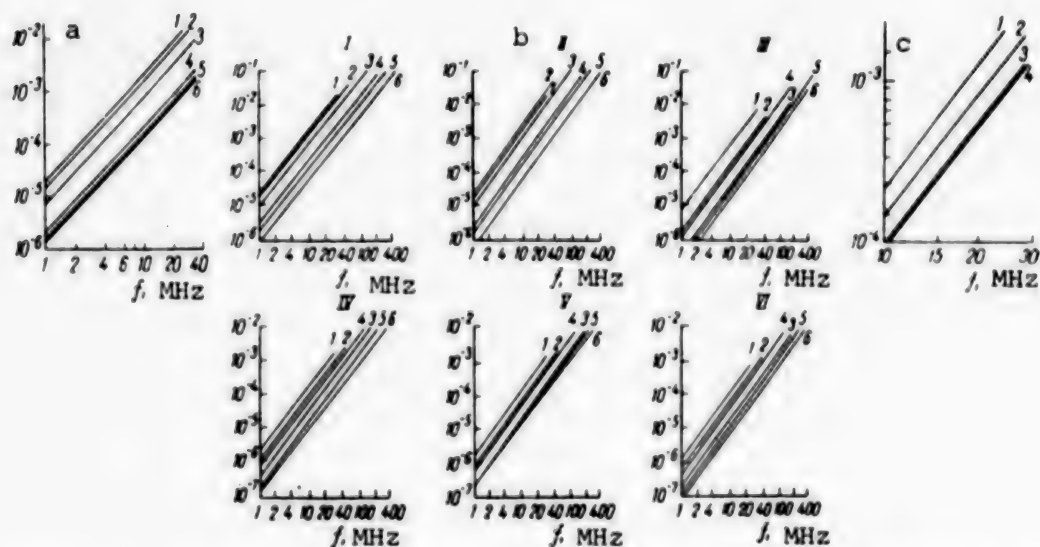


Figure 2. SAP averaged for mass as a function of EMO frequency during irradiation in free space from a field with intensity of 1 mW/cm^2 [51, 52]

- a) for models of average sized man with different polarizations
 - 1-6) polarization is EKH, EHK, KEH, KHE, HEK and HKE, respectively
- b) for models of different animal species with different polarizations
 - 1) man (average male)
 - 2) dog
 - 3) seated monkey
 - 4) rabbit
 - 5) rat
 - 6) mouse
- I-IV) EKH, EHK, KEH, KHE, HEK and HKE, respectively
- c) for models of different types of people (Table 3) with EKH polarization
 - 1) average male
 - 2) average female
 - 3) 10-year-old boy
 - 4) 5-year-old boy

X-axis, f (MHz), y-axis, SAP (W/kg)

For polarization $\vec{E} \parallel \vec{H}$ in the same range, one can use the empirically obtained equation [28]:

$$P_{am} = \frac{\Phi_1 \cdot (f^2/f_{res}^2)}{(f^2/f_{res}^2) + \Phi_2 \cdot [(f^2/f_{res}^2) - 1]^2}, \text{ W/kg} \quad (8)$$

where Φ_1, Φ_2 are quantities that depend on the dimensions of the spheroid used to approximate man or an animal and f is EMW frequency.

Table 3. Data for building ellipsoid models of man and laboratory animals [52]

| Object | Average weight, kg | Average height, m | a/b | b/c |
|---------------|--------------------|-------------------|------|-----|
| Average man | 70 | 1,75 | 4,48 | 2,0 |
| Average woman | 61,1 | 1,61 | 4,02 | 2,2 |
| Boy, 10 years | 32,2 | 1,38 | 4,93 | 1,8 |
| Boy, 5 years | 19,5 | 1,12 | 4,67 | 1,7 |
| Seated monkey | 3,5 | 0,40 | 2,53 | 1,5 |
| Dog | 15,0 | 1,12 | 5,92 | 1,4 |
| Rabbit | 1,0 | 0,40 | 5,52 | 1,1 |
| Rat | 0,2 | 0,15 | 2,54 | 1,4 |
| Mouse | 0,02 | 0,0536 | 1,73 | 1,4 |

Note: $a > b > c$ are ellipsoid semi-axes.

The empirical expressions obtained for the coefficients used may be useful in practical studies [28]:

$$\begin{aligned} \Phi_1 &= [-0,994 - 10,69a + 0,172(a/b) + \\ &\quad + 0,739(1/a) + 5,66(a/b^2)] \cdot 10^{-3}; \\ \Phi_2 &= [-0,91 + 41,4a + 399,17(a/b) - \\ &\quad - 1,2(1/a) - 2,14(a/b^2)] \cdot 10^{-3}; \\ \Phi_3 &= (-0,91 + 41,4a + 399,17(a/b) - \\ &\quad - 1,2(1/a) - 2,14(a/b^2)] \cdot 10^{-3}; \\ \Phi_4 &= |\epsilon/\epsilon_{20}|^{-1/4}; \\ \Phi_5 &= 4,822a - 0,835(a/b) - 8,733a^2 + \\ &\quad + 0,001575(a/b)^2 + 5,3688a^3; \\ \Phi_6 &= 0,3353a + 0,0753(a/b) - 0,804a^2 - \\ &\quad - 0,0075(a/b)^2 + 0,64a^3; \\ f_1/f_{res} &= -0,421a + 1,239(a/b) + \\ &\quad + 1,09a^2 - 0,2945(a/b)^2 + 0,0195(a/b)^3 \\ f_2/f_{res} &= 21,8a + 0,502(a/b) - 50,81a^2 - \\ &\quad - 0,068(a/b)^2 + 34,12a^3; \end{aligned} \quad (8a)$$

where a and b are given in meters, ϵ is dielectric constant of tissue, $\epsilon_{20} = 2/3$. The empirical equation for frequency of resonance absorption with EKH and EHK polarizations has the following appearance:

$$f_{res} = 2.75 \cdot 10^8 [8a^2 + \pi^2(a^2 + b^2)]^{-1/4}, \quad (9)$$

where a and b are the large and small semi-axes of the spheroid (in m).

Range III (see Figure 1) has the maximum energy absorption. In this range, in addition to the above-mentioned digital methods of calculation, several empirically derived functions were obtained to estimate resonance frequency and averaged SAP [24, 25, 62, 63]. For different types of polarization in free space with intensity of 1 mW/cm^2 falling on a human model of length L , the frequency of resonance absorption (f_{res}) and peak SAP averaged for body mass can be calculated using the following equations [24]:

$$\begin{aligned} EKH: P_{am} &= 0.218 \cdot \left(\frac{1.75}{L} \right); \\ KEH: P_{am} &= 0.215 \cdot \left(\frac{1.75}{L} \right); \\ KEH: P_{am} &= 0.071 \cdot \left(\frac{1.75}{L} \right); \\ KHE: P_{am} &= 0.047 \cdot \left(\frac{1.75}{L} \right); \\ HEK: P_{am} &= 0.043 \cdot \left(\frac{1.75}{L} \right); \\ HKE: P_{am} &= 0.037 \cdot \left(\frac{1.75}{L} \right). \end{aligned} \quad (10)$$

For polarizations EKH and EHK, $f_{res} = 67.9 \left(\frac{1.75}{L} \right)$. For the other polarizations, peak absorption is smooth and resonance frequency is in the following range:

$$f_{res} = (143 \div 171) \cdot \left(\frac{1.75}{L} \right). \quad (11)$$

For the most intensive energy absorption with orientation $\vec{E} \parallel \vec{L}$, SAP averaged for mass as a function of ratio of body length to radiation wavelength can be examined in two subranges [21, 24, 62] (see Figure 1).

IIIa. Subresonance region ($0.5 f_{res} < f < f_{res}$). For man in free space with incident 1 mW/cm^2 flat wave:

$$P_{am} = 5.2 \cdot \frac{L^3}{M} \cdot (f/f_{res})^{2.75}, \text{ W/kg} \quad (12)$$

For laboratory animals:

$$P_{am} = 8.3 \cdot \frac{L^3}{M} \cdot (f/f_{res})^{2.75}, \text{ W/kg} \quad (13)$$

IIIb. Supreresonance region ($f_{\text{res}} < f < 1.6 \cdot S_{\text{res}} \cdot f_{\text{res}}$). For man, the resonance section of energy absorption S_{res} and average SAP are determined using the following equations [24]:

$$\begin{aligned} S_{\text{res}} &= 1.52 \cdot \sqrt{L^3 \cdot M}, \\ P_{\text{am}} &= 5.95 \cdot 10^8 \cdot L/f \cdot M, \quad \text{W/kg} \end{aligned} \quad (14)$$

Similarly, for laboratory animals:

$$\begin{aligned} S_{\text{res}} &= 24.0 \cdot \sqrt{L^3 \cdot M}, \\ P_{\text{am}} &= 9.47 \cdot 10^8 \cdot L/f \cdot M, \quad \text{W/kg} \end{aligned} \quad (15)$$

where M is body mass. All of the used parameters are expressed in the SI system. The obvious noncoincidence of dimensionalities is due to the fact that these equations were obtained empirically.

In the resonance range of $f_1 < f < f_2$, where f_1 and f_2 are found from the above equations and function (9), the authors of [28] propose an empirical relation to determine SAP averaged for body mass, for biological objects approximated by spheroids of revolution situated in the field of a flat 1 mW/cm^2 wave with polarization $\vec{E} \parallel \vec{L}$:

$$P_{\text{am}} = \frac{\Phi_1 \cdot (f^2/f_{\text{res}}^2) \cdot [1 + \Phi_3 \cdot (f/f_{\text{res}})]}{(f^2/f_{\text{res}}^2) + \Phi_2 \cdot [(f^2/f_{\text{res}}^2) - 1]^2}, \quad \text{W/kg} \quad (16)$$

where Φ_1 , Φ_2 and Φ_3 are empirical coefficients found from the above expressions.

In range IV (see Figure 1) ($f \gg f_{\text{res}}$), the relative section of absorption is asymptotically close to 0.5. For all possible body orientations in space in relation to field polarization planes, there are insignificant differences between SAP averaged for the body. In this range, use of numerical methods of calculating SAP becomes virtually impossible. Use of methods of geometric optics [40, 44, 46] and calculations used in dosimetry and protection against ionizing radiation permits solving the dosimetric problem in this instance also. At superhigh frequencies, in the region where the wavelength is smaller than dimensions or radius of curvature of a biological object, total absorbed power (TAP) does not depend on body shape and will be proportionate to the area of its cross section (S) in a plane perpendicular to the direction of dissemination of EMW. Here, dielectric losses in tissues become significant and even prevalent, and there are also noticeable differences in properties of different tissues, so that the body can no longer be considered homogeneous. Moreover, one must take into consideration the reflection of field energy by the body surface, which is also a function of frequency. We can propose the following equation for total absorption of power:

$$P_a = (1 - \epsilon_{\text{ref}}) \cdot I \cdot S, \quad (17)$$

where k_{ref} is the coefficient of reflection on the air-skin interface, which is minimally dependent on frequency and conductivity of tissue in this range ($k_{\text{ref}} = 0.5 \pm 0.1$) [8-9, 45]. In this case, SAP averaged for volume will have the following appearance:

$$P_{\text{av}} \approx 0.5 \cdot I \cdot S/V. \quad (18)$$

At depth x SAP is described by the following expression:

$$P_v(x) = P_0 \cdot (1 - k_{\text{ref}}) \cdot e^{-2x/d} \quad (19)$$

where $P_0 = I \cdot S_{\text{ef}}$ is energy incident on body per unit time; S_{ef} is effective body absorption surface [26, 60, 64], or

$$P_v(x) = P_v(0) \cdot e^{-2x/d}, \quad (20)$$

where $P_v(0)$ is SAP on body surface and d is depth of field energy penetration.

The depth of EMF penetration in biological tissue (d) is inversely proportionate to the absorption coefficient and it is defined as the distance over which electric field amplitude diminishes by e times, while energy flux density (EFD) declines by e^2 times [8-9, 65]:

$$d = \lambda_0 [2\pi\epsilon (\sqrt{1 + \text{tg}^2 \delta} - 1)]^{1/2}, \quad (21)$$

where λ_0 is EMF wavelength in a vacuum, ϵ is relative dielectric permeability of tissue, $\text{tg} \delta$ is tangent of angle of loss ($\text{tg} \delta = \epsilon_1/\epsilon_2$; ϵ_1 and ϵ_2 are real and imaginary parts of combined dielectric permeability).

With penetration into tissue, there is a change in rate of dissemination of EMW in the medium and, consequently, in wavelength in tissue:

$$\lambda_{\text{ti}} = \lambda_0 \left[\frac{\epsilon}{2} (\sqrt{1 + \text{tg}^2 \delta} + 1) \right]^{-1/2}. \quad (22)$$

At very high frequencies, the square of the loss angle tangent is considerably smaller than 1, and according to (3) $\lambda_{\text{ti}} \approx \lambda_0 \sqrt{\epsilon}$. Equation (20) shows that the depth of EMF penetration into biological tissue will decrease with increase in wave frequency and will ultimately lead to superficial interaction of the field with a biological specimen. Due to high dielectric permeability, the wavelength in tissue is smaller than in vacuum (see Figure 2). This decline constitutes 6.5 to 8.5 times for tissues with high fluid content and 2 to 2.5 times for those with low fluid content [8-9, 65]. It is obvious that depth of EMF penetration into tissue will decrease with increase in frequency. Thus, 2.4 GHz microwaves can penetrate to a depth of 2 cm in tissue, while those of more than 10 GHz are absorbed primarily by the superficial layers of the human integument.

In this case, ($f > f_2$), and the authors of [28] propose an empirical equation for determination of SAP in the case of exposure in free space to a 1 mW/cm² flat wave for polarization $\vec{E} \parallel \vec{L}$:

$$P_{am} = \frac{\Phi_1 \left(\frac{f^2}{f_{res}^2} \right) \cdot [1 + \Phi_3 \cdot (f/f_{res})] + \frac{\Phi_4 \cdot \Phi_5 \cdot (f^2/f_{res}^2)}{+ \Phi_2 [(f^2/f_{res}^2) - 1]^2}}{(f^2/f_{res}^2) +} \quad \text{W/kg} \quad (23)$$

where f is EMO frequency, f_{res} is frequency of resonance energy absorption as defined in expression (9), $\Phi_1, \Phi_2, \Phi_3, \Phi_4, \Phi_5$ are coefficients that are found from the functions listed above. For $f \gg f_{res}$ empirical equation (23) is reduced to:

$$P_{am} = \frac{\Phi_1 \cdot \Phi_4 \cdot \Phi_5}{\Phi_2} \cdot \text{W/kg} \quad (24)$$

It should be noted that equation (24) does not depend on EMO frequency, but does depend on magnitude of dielectric permeability of tissue for the tested frequency, which is described by function Φ_5 . In real cases, when the medium consists of several layers of different tissues, the thickness of which is smaller than penetration depth, part of the EMO is reflected from the interface, and standing waves with absorption maximums they elicit may appear in tissues.

Thus, it is possible to assess SAP averaged for the entire body by a biological specimen in free space in the far zone of a flat EMW.

However, the distribution of SAP within the specimen is not uniform, and it depends on many factors. Maximum local absorption occurs not only because of presence of interfaces between tissues with different electrical properties. In a human body of complex configuration, there may be partial resonances on the limbs, which depend on the spatial position of the body and frequency of EMR waves. Each of the partial resonances determines both local absorption and overall redistribution of SAP.

Figure 3a illustrates frequency functions of averaged SAP in different parts of the body [63]. It should be noted that there are disproportionate frequencies of contributions of partial absorption in specific absorption of energy averaged for the whole body. For example, at frequencies of up to approximately 100 MHz, with lateral exposure to a flat ($\vec{E} \parallel \vec{L}$) polarized wave in free space, SAP in the human leg is greater by more than a factor of 10 than in the arm, whereas in the range of 100 to 300 MHz, SAP in the arm is already several times greater than absorption in the leg. There are several maximums of absorption, even by a homogeneous model of the human head [8-9, 38, 39, 66], and some researchers [41, 63, 67] define resonance frequency in this instance in the range of 300 to 400 MHz. We must stress that there is a difference in absorption by an intact model of the head and the head as part of a model of a whole human body [31, 68].

Under real conditions, there are frequent situations when man is exposed to radiation while in direct contact with the ground, rather than in free space. Figure 3b illustrates the averaged partial resonance SAP by a homogeneous model of a human being whose feet are in contact with the current-conducting

surface of the ground. Then the absorption peaks, which are somewhat redistributed, shift to the left in frequency. Insulating soles and platforms elevate all of the human body to a different altitude. Figure 3c gives an idea about the change in partial SAP as a function of position of a man standing erect in relation to the ground [48, 69]. Let us note that, in this case, SAP is several times greater at this frequency than with exposure in free space, and it reverts rather slowly to these levels with increase in distance to the grounded plane.

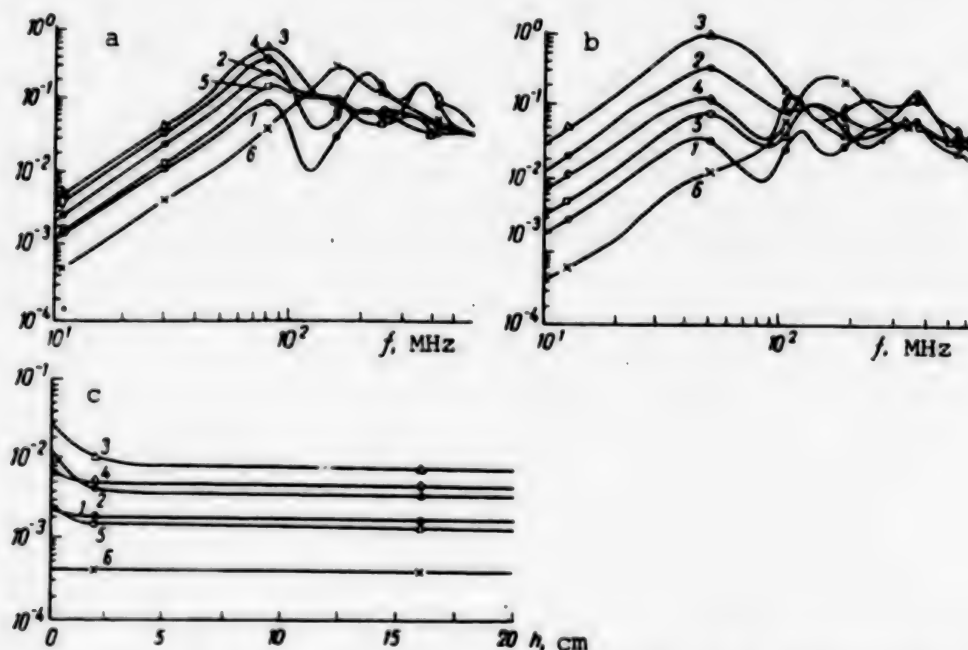


Figure 3. SAP in different parts of the human body averaged for mass, as a function of EMO frequency (a and b) and distance between feet and current-conducting surface (c) with 1 mW/cm^2 intensity of incident radiation [48, 62, 63]

- a) irradiation in free space
- b) irradiation with man's feet in contact with the ground
- c) EMF irradiation at frequency of 10 MHz
- 1) head
- 2) average for body
- 3) leg
- 4) neck
- 5) trunk
- 6) arm

Y-axis, SAP (in W/kg)

SAP changes significantly when biological objects are situated in the vicinity of vertical reflecting planes. Thus, at frequencies near resonance for the whole body with $\vec{E} \parallel \vec{L}$ orientation, absorption by a body that is before the conducting plane increases by almost 7 times, as compared to SAP in a free field. At high frequencies, the multiplicity of increase (η) asymptotically tends towards 2. An even greater SAP is observed when the body is placed in the line of a rectangular reflector [48, 62, 70]. Analogously to a flat reflector, at high frequencies η tends asymptotically toward a constant value of about 8.

Close to resonance with $\vec{E} \parallel \vec{L}$ orientation, there was even greater increase in SAP, as compared to SAP in free space ($\eta \approx 27$). Other exotic combinations of reflective surfaces could be offered, which lead to even greater increase in SAP by biological objects.

In addition to the above factors (difference in dielectric characteristics of tissues, polarization, partial resonance, "grounding" effect, presence of reflective surfaces), the dimensions and construction of emitting unit, distance to EMR source, as well as type of excited wave, affect distribution of SAP in a biological object. However, a number of recent theoretical and experimental studies dealing mainly with slit, aperture and dipole emitters [54, 71, 72] demonstrated that it is possible to use the above-described methods for evaluation of SAP in animal and human models exposed to the near zone of radiation. In more complicated situations, it is promising to use direct experimental methods to examine endogenous fields and distribution of SAP.

The above dosimetric analysis of EMF interaction with biological objects leads us to conclude that classification of intensities of incident EMR as "thermal" and "nonthermal" without consideration of concrete interaction conditions is arbitrary [1, 8-9, 73]. Even in free space, a flat wave of the same intensity could have both a substantial and very insignificant thermal effect, depending on irradiation conditions. In living biological systems, the adaptability of organs and tissues to thermal loads depends, of course, on their basal metabolic rate. And local heating should be expected if EMF-induced heat emission is comparable to metabolism at the tested point. One must also take into consideration elimination of effects which arise when the body is exposed to electromagnetic radiation [74, 75]. All this requires consideration of effective dosage [74, 76].

Using the data in Table 2, one can apply the energy-frequency method of extrapolating biological effects from animals to man. Let us assume that a certain biological effect is observed when rats are exposed to EMF at intensity of 10 MW/cm^2 and frequency of 2.4 GHz. In order to find the EMR parameters that would lead to the same biological effect in man (provided geometric parameters of interaction are adhered to), let us perform the following operations. In order to have local SAP distribution that is approximately analogous, we need to adhere to the following equation [57]:

$$L_1/\lambda_1 = L_2/\lambda_2, \quad (25)$$

where L_1 and λ_1 are wave size and length, which determine the process of energy absorption in an object with known biological effect; L_2 and λ_2 are the same characteristics for inducing an analogous biological effect on the species to which the effect is being extrapolated.

We find from Table 3 the average dimensions of man ($L_2 = 1.75 \text{ m}$) and rat ($L_1 = 0.15 \text{ m}$). A 2.4 GHz frequency corresponds to a wavelength of $\lambda_1 = c/f = 0.125 \text{ m}$. From equation (25) we find that $\lambda_2 = \frac{L_2 \cdot \lambda_1}{L_1} = 1.458 \text{ m}$, which corresponds to a frequency of about 260 MHz. According to Table 3, the averaged SAP for both rats and man is determined in interval IIIb using formulas (14) and

(15). For a rat, with 10 mW/cm^2 incident flat wave (2.4 GHz), P_{at}^* equals 0.296 W/kg . An intensity of 10 mW/cm^2 will elicit SAP averaged for rat mass equaling 2.96 W/kg . For man, a flat wave at a frequency of 206 MHz and intensity of 1 mW/cm^2 elicits P_{at}^* of 0.072 W/kg , and the calculation is made using formulas (14) and (15).

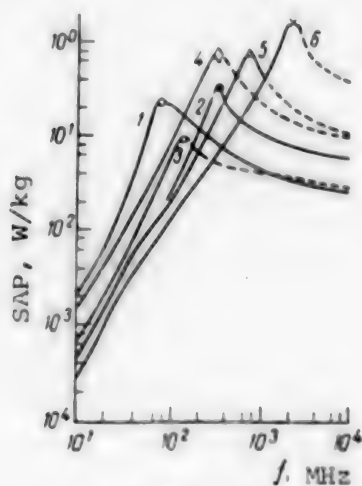


Figure 4.

Frequency as a function of SAP averaged for body mass in homogeneous models of man and some laboratory animals placed in field of flat 1 mW/cm^2 EMW with $\vec{E} \parallel \vec{L}$ polarization [8]

- | | |
|-----------|-----------|
| 1) man | 4) rabbit |
| 2) monkey | 5) rat |
| 3) dog | 6) mouse |

similar spatial distribution in the body, a field intensity of about 40 mW/cm^2 at a frequency of 206 MHz is needed. Without consideration of frequency modeling, it can be stated that, at a frequency of 2.4 GHz an intensity of about 75 mW/cm^2 elicits the same effect in man as in a rat at field intensity of 10 mW/cm^2 .

The data in Figure 4, which illustrates frequency as a function of averaged SAP in homogeneous spheroid models of man and some laboratory animals placed in a flat EMW field of 1 mW/cm^2 at $\vec{E} \parallel \vec{L}$ polarization [8-9], may be useful for rougher estimates of SAP averaged for body mass in the frequency range of 10 to 10^4 MHz with use of the proposed method. In this range, these functions permit evaluation of SAP for different animal species and man after preliminary frequency modeling of equivalence of local SAP (ratio 25).

On the basis of analysis of processes of energy absorption, we can suggest an approach to assessment of hazard of both a monochromatic and mixed EMR spectrum. By introducing the concept of coefficient of irradiation quality (k_q), defined

Table 4.

Coefficients determining quality of irradiation as a function of frequency range and type of polarization

| Polarization | Coefficient | Frequency range, MHz | | |
|--------------|-------------|----------------------|----------------------|-----------|
| | | $1 < f < 30$ | $30 \leq f \leq 300$ | $f > 300$ |
| \vec{E} | η_1 | 0.5 | 8 | 1 |
| | η_2 | 1 | 25 | (*) |
| | η_3 | 10 | 5 | 1 |
| \vec{k} | η_1 | 0.25 | 3 | 1 |
| | η_2 | 1 | 10 | (*) |
| | η_3 | 3 | 2 | 1 |
| \vec{H} | η_1 | 0.05 | 1.25 | 1 |
| | η_2 | 1 | 10 | (*) |
| | η_3 | 3 | 2 | 1 |

(*) reflecting surfaces could form various configurations (to focusing); in this range, coefficient η_2 should be determined by conditions of geometrical optics

Thus, in order to create SAP in the human body analogous to SAP in a rat with

*Translator's note: Subscript "at" may be typo for subscript "am."

as the ratio of intensity of exemplary irradiation generating a specific SAP in a biological specimen to intensity of such irradiation eliciting the same SAP, we can turn to the concept of effective intensity of irradiation (I_e), which is found from the formula, $I_e = k_q I$, where I is intensity of incident EMR. For man, one should consider irradiation of a given biological object in a free EMO field of 2.4 GHz as the exemplary (standard) irradiation, which is widely used in practice. Analysis of conditions of formation of SAP revealed that the coefficient of quality is a function of EMO (η_1), presence of reflective surfaces (η_2) and electric contact with the ground (η_3). Consequently, we can write down:

$$I_e = \eta_1(\vec{E}, \vec{k}, \vec{H}) \cdot \eta_2(\vec{E}, \vec{k}, \vec{H}) \times \eta_3(\vec{E}, \vec{k}, \vec{H}) \cdot I, \quad (26)$$

where $\eta(\vec{E}, \vec{k}, \vec{H})$ means that the coefficient depends on type of polarization.

Table 4 lists the estimated maximum values for the above coefficients for the cases of human exposure to radiation that may be encountered in practical studies.

At frequencies under 1 MHz, the coefficient of irradiation quality is less than 10^{-3} , the deciding role in the process of energy absorption belongs to the grounding effect and induced superficial current, the values of which must be determined using formula (6) in each case. Analogously, in the super-high-frequency range, the presence of reflective surfaces could become a factor that determines the nature of EMR energy absorption by the body.

As an example, let us find the effective intensity of radiation at a frequency of 70 MHz with E polarization for a man that is in front of reflective screens and in electric contact with the ground. $I_e = 1000 \cdot H$. This means that, in order to obtain SAP that is approximately equivalent to standard irradiation and under the discussed conditions, only one-thousandth the intensity of standard radiation is required. For example, exposure of man to EMF with intensity of 10 mW/cm^2 at a frequency of 2.4 GHz in free space creates approximately the same SAP as exposure under the conditions discussed (70 MHz, E polarization, grounded, reflection) with incident EMR intensity of $10 \text{ }\mu\text{W/cm}^2$. This case is the maximum of all possible qualities of irradiation conditions.

Estimation of the hazard of a complex EMR spectrum can be made by the method of competing frequencies or bands [76]. In general, in the presence of a series of m competing frequencies, the intensity of which is measured in V/m, and a series of k frequencies, the intensity of which is measured in W/cm^2 , irradiation may be considered safe if the following condition is satisfied:

$$\sqrt{\sum_{i=1}^m \left(\frac{E_i}{E_{i\text{per}}} \right)^2} + \sum_{i=1}^k \left(\frac{I_i}{I_{i\text{per}}} \right) \leq 1, \quad (27)$$

where E_i is intensity of electric component of field for i th frequency band; I_i is intensity of i th frequency band, $E_{i\text{per}}$ is regulated maximum permissible

intensity of electric field for i th frequency; $I_{i\text{per}}$ is regulated maximum permissible intensity of i frequency.

In conclusion, we can mention several problems related to biophysics of EMF interaction with the body that require further development. For example, estimation of biological effectiveness and modeling when an object is in the near zone of electromagnetic sources. It is not so much the theoretical estimates that are of great importance (since they are very complicated) as modeling the biological effects under actual exposure conditions. Estimation of biological effectiveness of EMR in the presence of other objects with radioabsorbing and reflective properties also presents a difficult dosimetric problem. Finally, it is of definite interest that physiologically significant structures (reflexogenic zones) are heterogeneous in estimating local SAP and EMR dosimetry in the case of nonuniform irradiation: local shielding or local irradiation.

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EXPERIMENTAL AND GENERAL THEORETICAL RESEARCH

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MAIN RESULTS OF MEDICAL STUDIES ON SALYUT-6--SOYUZ PROGRAM

Moscow KOSMICHESKAYA BIOLOGIYA I AVIAKOSMICHESKAYA MEDITSINA in Russian Vol 18, No 2, Mar-Apr 84 (manuscript received 19 Aug 82) pp 22-25

[Article* by Ye. I. Vorob'yev, O. G. Gazenko, A. M. Genin, N. N. Gurovskiy, A. D. Yegorov and Yu. G. Nefedov]

[English abstract from source] In 1977-1981 the Soviet Union launched 18 manned space missions under the Salyut-6--Soyuz program which included five flights of prime crews for 96, 140, 175, 185 and 75 days and eleven flights of visiting crews. Altogether 30 cosmonauts, including 9 crewmembers from other than the USSR socialist countries, took part in the program. Emphasis was given to the medical investigations, since their purpose was not only to assess the health status of the crewmembers and to investigate their responses to prolonged weightlessness, but also to identify the maximum allowable flight time.

[Text] In 1977-1981, 18 manned flights were launched in the Soviet Union on Salyut-6--Soyuz programs: 5 flights of primary missions lasting 96, 140, 175, 185 and 75 days, and 11 rendezvous missions. A total of 30 cosmonauts participated in the program, including 9 cosmonauts from socialist countries. Medical studies occupied a special place in the Salyut-6--Soyuz program, since they included not only ongoing evaluation of the crew's health status and investigation of phenomenology of reactions to long-term weightlessness, but determination of the maximum safe long-term spaceflights.

The cosmonauts' work capacity was adequate during the missions. The initial manifestations of effects of weightlessness were characterized by appearance in some cosmonauts of brief spatial illusions and consistent development of sensation of blood rushing to the head. In some cases, there were more or less marked symptoms of motion sickness. All these signs varied in severity and duration, and they usually leveled off or disappeared in the 1st week

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of the flight. Some cosmonauts did not develop any unpleasant sensations during adaptation to weightlessness.

In most cases, the cosmonauts lost a maximum of 1.4-5.4 kg during long-term missions. However, this parameter exceeded the preflight level for the flight engineer on the 175- and 185-day missions and commander of the 185-day mission. Volume of the lower leg consistently decreased inflight in all cosmonauts. Redistribution of blood to the upper part of the body, loss of body fluids, reduction in muscle mass due to deconditioning, as well as, probably, the periods of increased physical and emotional activity (for example, extra-vehicular activity during the "Vykhod" [exit] operation), inadequate food intake for different reasons (for example, selective lessening of appetite for certain foods), could have been the possible causes of decrease in body weight and leg volume. At the same time, the noted cases of weight gain inflight are indicative of the possibility of compensation and even exceeding metabolic loss with the food allowance (provided a good appetite was retained due to the gustatory qualities of rations) and adequate fluid intake.

In the set of medical studies, special attention was given to the body systems that were assumed to undergo substantial changes in the course of a long-term spaceflight. It was important to determine whether such changes could develop to an extent that would prevent extending spaceflights.

The results of examination of the cardiovascular system revealed that in weightlessness there is redistribution of delivery of blood to different regions, and it has a tendency toward leveling off with increase in flight duration due to reduction in volume of circulating blood and redistribution of vascular tonus. The reactions of the cardiovascular system, when tested at rest and during functional tests in flight, became stabilized. Moreover, wise and regular use of the set of preventive measures could turn out to be so effective that the circulatory system reactions to inflight functional tests would be the same as in preflight tests. Thus, during the 175-day mission and in some of the tests done in the 185-day flight, tolerance of physical load tests was rated as good, while the intensity of circulatory reactions was the same as preflight. However, after the missions, all cosmonauts presented signs of orthostatic and physical deconditioning, which did not last long and did not exceed in severity the changes observed following short-term flights.

Among the most relevant findings made in studies of hemodynamics during long-term flights is demonstration of the fact that approximately the same venous pressure is established in vessels of the forearm, lower leg and jugular veins. This finding is of substantial significance to comprehension of hemodynamic changes that develop in weightlessness and to their specific prevention.

The obvious effects of weightlessness on the motor system were usually manifested by some loss of muscle mass, visible atrophy of muscles of the lower extremities, long and short muscles of the back, as well as decreased muscle tone and strength of antigravity muscles. Testing of the tendinal T reflex of the gastrocnemius revealed a postflight decline of response threshold and decrease in maximum amplitude of the reflex, with distinct depression of mechanisms of interactions between extremities. The system of motor regulation

underwent a number of changes postflight: increased share of high-frequency oscillations on the stabilogram, longer time for restoration of equilibrium after exposure to exogenous involuntary perturbances, increased amplitude of myographic responses of crural muscles. The severity and duration of motor disturbances depended on the type of program of preventive measures. Thus, after the 175-day mission, there was no noticeable loss in muscle mass, with the exception of some muscles that organize head-holding and muscles of the shoulder girdle. More marked changes in the muscular system were found after the 185-day flight than the 175-day one. Evidently, this is attributable to more complete performance of conditioning procedures in the 175-day mission, particularly the strength exercises with the expander, which are apparently very important in this situation.

Biochemical tests revealed that there was some postflight decrease in intensity of oxidative processes in the body with concurrent increase in share of anaerobic conversions in the overall sum of energetic reactions. There was also activation of the sympathoadrenal system (SAS) after the missions. There was usually prevalence in activity of the adrenal part of the SAS, although in some cases activation of the mediatory element of SAS was observed. The postflight changes in levels of hormones and biologically active compounds in body fluids are presently viewed as adaptive reactions aimed at maintaining a number of body functions on a certain level, for example, fluid-electrolyte metabolism (changes in activity of the renin-angiotensin system), vascular tonus and orthostatic stability (changes in levels of cyclic nucleotides and prostaglandins). However, the significance of these changes could not always be interpreted, and it is largely determined by individual distinctions of the body.

The postflight changes in fluid-electrolyte metabolism were most often manifested by diminished excretion of fluid and sodium, increased excretion of potassium and calcium in urine. The changes in blood electrolyte concentrations were usually minor and as a rule they were manifested by significant decrease in potassium content. At the same time, following the 185-day mission, a decrease in total calcium and its ionized fraction in blood combined with a negative calcium balance was observed for the first time. This merits close attention. Water and salt load tests revealed postflight lack of coordination in the ion-regulating system.

The changes in fluid-electrolyte metabolism were transient, and they could have been due to changes in the system of regulation and hormonal status in weightlessness and during readaptation to earth's conditions. It is also possible that the decrease in the potassium pool of cells was due to metabolic changes in the muscular system. It should be noted that increased excretion of potassium in the presence of hypokalemia and calcium with decline of its level in blood, as observed after the 185-day flight, were probably related to inability of muscle tissue to retain ions as a result of atrophic processes, which develop due to insufficient load on the skeletomuscular system in weightlessness.

Loss of calcium and other mineral components of bone tissue could be a substantial factor with regard to limiting the possibility of continuing a spaceflight. It has been shown that the decrease in mineral components of the calcaneus did not exceed 3.2-8.8% after 6-month missions, which is

substantially less than after long-term bed rest. These figures correspond to mineral loss after 3-month flights. Thus, it was shown that one can apparently stabilize mineral component content of the calcaneus by means of intensive conditioning of the crew.

Hematological studies are of great scientific interest, since it had been shown previously that there is substantial postflight decline of erythrocyte mass. Since the average life span of erythrocytes is 120 days, there should have been complete renewal of these cells in a 140-180-day flight. If weightlessness impaired the process of formation and development of erythrocytes, it would lead to development of severe forms of anemia. After long-term flights, a decrease in erythrocyte count and hemoglobin was demonstrated, which did not present a clearcut dependence on flight duration, but progressed for some time after termination of the flight. These hematological parameters recovered within about 1.5 months after flights.

According to current conceptions, these changes are related to compensatory decrease in inflight circulating blood volume and considerably faster restoration of blood plasma than erythrocytes after flights. The demonstrated structural changes in erythrocytes were quite moderate and did not progress with increase in flight duration. The findings permit an optimistic assessment of the possibility of adaptation of the blood system to conditions of long-term spaceflights and its recovery in the postflight period.

Immunological studies revealed that there are consistent changes following long-term flights: decrease in blood T lymphocyte content, diminished reactivity of these immunocompetent cells and capacity for proliferation. The first studies to be made after the 185-day flight demonstrated a decrease in activity of T helpers and natural killers, with unchanged suppressor activity. The findings indicate that immunological reactivity of the body changes under the influence of conditions of long-term spaceflights, with gradual normalization during the readaptation process.

In conclusion, it should be noted that the cosmonauts failed to demonstrate any serious diseases during the manned flights in the Salyut-6--Soyuz orbital complex. There were only isolated cases of minor ordinary trauma. The demonstrated changes in composition and quantity of autogenous microflora, microflora of cabin air and surfaces did not present an appreciable threat with respect to infectious diseases.

The general result of these medical studies is establishment of the fact that when spacecraft crews perform a special program of exercise and adhere to satisfactory living conditions and optimum work and rest schedule, none of the physiological changes found after short-term spaceflights progressed when flight duration was increased from 1 month to 6 months. This circumstance enables us to make an optimistic assessment of the prospects of further extending flight duration.

Virtually no serious psychological problems have occurred in any of the flights made to date, that would have hindered performance of assignments or led to psychological disorders. This was achieved by the high motivation of crews,

effectiveness of psychological screening, satisfactory living conditions in spacecraft, balanced schedule of work and rest, as well as special measures for psychological support of the crews.

Nevertheless, we must realize the seriousness of these problems, particularly when the mission takes place under particularly dangerous conditions or makes very high demands as to quality of operator performance by the crew. Additional sociopsychological and ethical problems arise in the case of long-term spaceflights, and their solution could ultimately remain as the most important factor limiting the duration of future manned space missions.

Preservation of a good physical condition and high work capacity during long-term spaceflights, as well as rather smooth and easy progress of readaptation process following such flights, are the result of medical control used during the flights with a set of preventive agents based on periodical medical examinations of the crews in the course of the flights. It was also aided by a wise work and rest schedule, proper nutrition, adequate fluid intake and sufficient sleep. The results of these studies revealed that the course of the postflight readaptation period depends on the scope of preventive measures: the more actively and fully the crewmembers performed preventive procedures aboard the spacecraft, the more and better preservation of their functional capacities after the flights.

It is important to note that the flight engineer participated in the 185-day mission 6 months after a 175-day flight. His general condition and work capacity were virtually the same in both missions. This is indicative of absence of long-term aftereffects from stressors, with which long-duration spaceflights are related. After a 6-month intermission, there was sufficient recovery of body functions to permit going on a second, even longer spaceflight.

BLOOD PLASMA FREE AMINO ACID LEVELS IN COSMONAUTS BEFORE AND AFTER 175-DAY MISSION ABOARD SALYUT-6

Moscow KOSMICHESKAYA BIOLOGIYA I AVIAKOSMICHESKAYA MEDITSINA in Russian Vol 18, No 2, Mar-Apr 84 (manuscript received 3 Feb 83) pp 26-33

[Article by I. G. Popov and A. A. Latskevich]

[English abstract from source] Measurements of 17 free amino acids were performed before and after the Salyut-6 175-day spaceflight. At R+1 both crewmembers showed a reduced concentration of most amino acids as compared to the preflight level. By R+7 the preflight status was not yet reached. It is recommended to enrich the space diet with the following essential amino acids: preflight--methionine, leucine, isoleucine, phenylalanine, lysine, threonine, cystine and tyrosine; postflight--lysine threonine, valine, leucine, isoleucine, phenylalanine, methionine and cystine.

[Text] Investigation of the effects of living conditions during spaceflights on metabolism of flight vehicle crewmembers is still one of the pressing tasks for space biology and medicine. Among other types of metabolism, the dynamics of protein metabolism require further studies. This is needed, both in the interests of deeper physiological evaluation of this key element of human and animal metabolism under the unique conditions of spaceflights with unusual combination of anabolic and catabolic processes, and in the interests of upgrading nutrition and other life-support systems, as well as agents for the prevention of consequences from exposure to flight factors.

We submit here the results of assaying free amino acids in blood plasma of the commander (CDR) and flight engineer (FLE) before and after their 175-day mission aboard the Salyut-6 orbital research station. The results of this study enlarge upon data about the dynamics of blood amino acids in cosmonauts under the effect of spaceflights of different duration, as well as a number of concomitant factors, including diet, previously published by A. S. Ushakov, T. F. Vlasova [1, 2] and us [3-6].

Methods

The levels of 17 free amino acids in blood plasma of cosmonauts were assayed before the mission in the period of preflight training, during a routine

clinical and physiological examination, then on the 1st and 7th days after termination of 175-day flight. Venous blood samples were drawn and processed by standard methods. Amino acids were assayed with a Hitachi model KLA-3B automatic analyzer [7, 8]. The amino acid concentrations found were analyzed by comparing them to data listed in known textbooks [9-14] and experimental works [1, 2], as well as the results of our tests on other cosmonauts before and after missions aboard Salyut-5 and Salyut-6 stations [3-6].

Results and Discussion

Table 1 lists the results of assaying 17 free amino acid levels in blood plasma of the CDR and FLE of the Salyut-6 orbital research station before and after their 175-day mission.

The concentrations of most blood plasma amino acids preflight in both cosmonauts were in the range cited by I. S. Balakhovskiy in the latest, 3d edition, of "Bol'shaya meditsinskaya entsiklopediya" (BME) [Great Medical Encyclopedia] as "approximate plasma levels in adults" of free amino acids [9]. Only methionine, cystine, aspartic acid in CDR and methionine, cystine, arginine, aspartic acid in FLE were below the bottom of the range of physiological fluctuations in healthy adults. The concentrations of methionine and arginine were insignificantly lower than the above-mentioned bottom of the normal range, while concentrations of cystine and aspartic acid differed more appreciably in the cosmonauts.

Aspartic acid concentration was 1.78 mg% lower in the CDR and 1.73 mg% lower in the FLE, or 89 and 86.5% respectively, as compared to the bottom of the range of physiological fluctuations [9]. However, it should be noted that the physiological range listed in BME appears to be somewhat high. In another, rather authoritative textbook by Muller [10], considerably lower values are listed as the physiological norm, from traces to 0.72 mg%. Several authors also cite lower figures as the norm: 0.01-0.07 mg% [11, 12]. A. S. Ushakov and T. F. Vlasova [1, 2], who examined cosmonauts, found 0.11 ± 0.01 mg% and even 0.07 ± 0.05 mg% aspartic acid, which is also considerably less than the BME standard. It is close to the concentrations for cosmonauts listed in Table 1, and even lower than the latter. When we tested other cosmonauts during training for missions lasting for different periods of time, we found concentrations of 0.11 and 0.32 mg% [3], 0.14 and 0.21 mg% [5], 0.22 and 0.19 mg% [6] in the CDR and FLE, respectively. All this compels us to consider the "approximate values" for blood plasma aspartic acid listed in BME to be too high, and this does not give us sufficient grounds to conclude that the concentration of this amino acid was low in the tested crewmembers of Salyut-6 prior to the 175-day mission.

In both cosmonauts, methionine concentration was slightly below the bottom of the physiological range according to I. S. Balakhovskiy [9], B. I. Zbarskiy [13] and N. V. Semenov [11], but higher than the bottom of the normal range according to Muller [10]. A. S. Ushakov and T. F. Vlasova cite values that are both lower than ours-- 0.26 ± 0.01 mg% [1]--and higher concentrations-- 0.54 ± 0.04 mg% [2]. This suggests that, according to the data of most authors, preflight methionine content of plasma was at a relatively low level in both cosmonauts, close to the bottom of the normal range.

Table 1. Free amino acid content (mg%) in blood plasma of crewmembers of Salyut-6 orbital research station before and after 175-day mission

| Amino acids | CDR | | | | | | FLE | | | | Approx. levels in adult plasma according to I. S. Balakhovskiy | | Levels in plasma of adults according to Muller | |
|---------------|-----------|---------------------|----------------------|----------------------------|---------------------|-----------|---------------------|----------------------|----------------------------|---------------------|--|------|--|------|
| | preflight | 1st post-flight day | inflight change, mg% | inflight change, % of base | 7th post-flight day | preflight | 1st post-flight day | inflight change, mg% | inflight change, % of base | 7th post-flight day | scatter | mean | physiol. range | mean |
| | | | | | | | | | | | | | | |
| EA: | | | | | | | | | | | | | | |
| lysine | 2.76 | 1.69 | -1.05 | -38.0 | 2.19 | 3.42 | 2.21 | -1.21 | -35.4 | 1.98 | 1.0-4.0 | 2.5 | 2.11-3.09 | 2.54 |
| threonine | 2.98 | 2.45 | -0.53 | -18.8 | 3.67 | 2.48 | 0.91 | -1.57 | -63.3 | 2.23 | 1.0-3.0 | 2.0 | 1.22-3.93 | 1.94 |
| valine | 2.02 | 1.91 | -0.11 | -5.4 | 1.99 | 1.98 | 2.20 | +0.22 | +11.1 | 1.72 | 1.5-3.0 | 2.3 | 1.36-2.66 | 1.99 |
| methionine | 0.29 | 0.10 | -0.19 | -65.5 | 0.37 | 0.27 | 0.22 | -0.05 | -18.5 | 0.31 | 0.3-0.7 | 0.5 | 0.23-0.39 | 0.32 |
| leucine | 1.82 | 0.91 | -0.91 | -50.0 | 1.33 | 1.38 | 1.26 | -0.12 | -8.7 | 1.09 | 1.0-3.0 | 2.0 | 0.93-1.78 | 1.32 |
| iso-leucine | 0.97 | 0.49 | -0.48 | -49.5 | 0.96 | 0.87 | 0.57 | -0.30 | -34.5 | 0.54 | 0.5-1.0 | 0.75 | 0.46-1.15 | 0.71 |
| phenylalanine | 0.94 | 0.53 | -0.41 | -43.6 | 0.80 | 0.84 | 0.66 | -0.18 | -21.4 | 0.63 | 0.5-2.0 | 1.25 | 0.63-1.92 | 0.95 |
| NA: | | | | | | | | | | | | | | |
| cystine | 0.78 | 0.63 | -0.15 | -19.2 | 0.68 | 0.74 | 0.70 | -0.04 | -5.4 | 0.32 | 1.0-3.0 | 2.0 | 1.15-3.37 | 1.77 |
| tyrosine | 1.19 | 0.57 | -0.62 | -52.1 | 0.99 | 0.72 | 0.56 | -0.16 | -22.2 | 0.83 | 0.6-2.0 | 1.3 | 0.65-1.13 | 0.91 |
| alanine | 3.12 | 3.45 | +0.33 | +10.5 | 3.32 | 3.19 | 2.11 | -1.08 | -33.8 | 3.59 | 2.0-4.0 | 3.0 | 2.22-4.47 | 3.07 |
| arginine | 1.32 | 0.86 | -0.46 | -34.8 | 1.13 | 0.96 | 0.84 | -0.12 | -12.5 | 1.02 | 1.0-3.0 | 2.0 | 0.86-2.63 | 1.48 |
| aspartic acid | 0.22 | 0.09 | -0.13 | -59.1 | 0.13 | 0.27 | 0.21 | -0.06 | -28.5 | 0.14 | 2.0-5.0 | 3.5 | trace 0.7 | 0.22 |
| histidine | 1.02 | 0.72 | -0.30 | -29.4 | 0.89 | 0.88 | 1.11 | +0.33 | +37.5 | 0.87 | 0.80-2.0 | 1.14 | 0.97-1.45 | 1.24 |
| glycine | 1.66 | 1.08 | -0.58 | -34.9 | 1.02 | 1.21 | 1.21 | none | none | 1.20 | 1.0-4.0 | 2.5 | 1.08-3.66 | 1.74 |
| glutamic acid | 2.13 | 1.78 | 0-35 | -16.4 | 1.69 | 2.04 | 1.44 | -0.60 | -29.4 | 3.05 | 0.7-4.0 | 2.3 | 0.25-1.73 | 0.86 |
| proline | 2.15 | 1.38 | -0.77 | -35.8 | 1.76 | 2.48 | 0.86 | -1.62 | -65.3 | 1.39 | 0.5-3.0 | 1.7 | 1.28-5.14 | 2.71 |
| serine | 1.66 | 0.82 | -0.84 | -50.6 | 1.68 | 1.49 | 0.88 | -0.61 | -40.9 | 0.78 | 1.0-2.0 | 1.5 | 0.68-2.03 | 1.18 |

Table 2. Summary indicators (mg%) of levels of 17 blood plasma amino acids in crew of Salyut-6 orbital research station before and after 175-day mission

| Indicator of amino acid metabolism | CDR | | | | | | FLE | | | | Approx. levels in adult plasma according to I.S. Balakhovskiy | | Levels in plasma of adults accord. to Muller | |
|---|-----------|----------------------------|----------------------------|----------------------------------|----------------------------|-----------|----------------------------|----------------------------|-------------------------------------|----------------------------|---|-------|---|-------|
| | preflight | 1st post- flight day | intlight change, mg% | intlight change, % of base | 7th post- flight day | preflight | 1st post- flight day | intlight change, mg% | intlight change, % of base | 7th post- flight day | scatter | mean | physiolog. range | mean |
| | | | | | | | | | | | | | | |
| Total amino acids | 27,03 | 19,46 | -7,57 | -28,0 | 24,61 | 25,21 | 17,95 | -7,26 | -28,8 | 21,69 | 16,40-48,70 | 32,55 | 16,08-40,25 | 26,16 |
| Total EA | 11,78 | 8,07 | -3,71 | -31,5 | 11,31 | 11,24 | 8,03 | -3,21 | -28,5 | 8,50 | 5,80-16,70 | 11,25 | 6,94-13,92 | 10,43 |
| Total NA | 15,26 | 11,38 | -3,88 | -25,4 | 13,30 | 13,97 | 9,92 | -4,05 | -29,0 | 13,19 | 10,60-32,0 | 21,30 | 9,14-26,33 | 17,73 |
| EA/NA ratio | 0,77 | 0,71 | -0,06 | -7,8 | 0,85 | 0,80 | 0,80 | none | none | 0,64 | 0,54-0,52 | 0,53 | 0,75-0,52 | 0,63 |

Cystine level was also below the bottom of the normal range in both cosmonauts [9, 10, 13, 14], and to an even greater extent than methionine. A. S. Ushakov and T. F. Vlasova cite figures that are close to our data: 0.73 ± 0.04 mg% [1] and 0.91 ± 0.10 mg% [2]. Cystine metabolism is closely related to that of methionine. When there is insufficient intake of cystine with food, it is synthesized from methionine. For this reason, the relatively low cystine level in plasma of both cosmonauts could be due to insufficient intake of this amino acid with food. Under such conditions, synthesis of cystine and methionine apparently did not compensate fully for insufficient intake with food. In turn, the greater outlay of methionine for cystine synthesis due to insufficient intake of the latter with food resulted in a low level of blood plasma methionine in both cosmonauts. In general, we had made analogous findings in testing other crews of Salyut-6 and Salyut-5 [3-6].

Plasma arginine level was slightly under the bottom of the normal range recommended in several textbooks [9, 11-14] only in the FLE. According to Muller, arginine concentration was in the normal range in the FLE [10]. When we tested other cosmonauts, we had found a somewhat low plasma arginine content in the CDR of Salyut-5 (second mission)-- 0.92 mg% [3] and CDR of Salyut-6 before the 140-day flight-- 0.97 mg% [6]. Arginine concentration was in the normal range in the rest of the members of these crews [9-14]. Evidently, it is a question here of both individual dietary distinctions and specifics of metabolism. This question requires clarification.

Concentrations of lysine, threonine, isoleucine, alanine and proline were above the averages in BME [9] in the CDR and FLE, whereas valine, leucine, phenylalanine, tyrosine, histidine, glycine and glutamic acid were below mean values. Evidently, identical

vital functions and diet resulted in similar levels of the above amino acids preflight in both cosmonauts' blood plasma.

Consequently, in both cosmonauts, preflight levels of 6 amino acids were above the average in the physiological range, while those of 11 amino acids were below the average level, and two of them, methionine and cystine, showed a concentration that was below the bottom of the normal range according to [9, 11, 13, 14]. We had previously observed a somewhat low methionine and cystine content of plasma in the preflight period in other cosmonauts [3-6], so have A. S. Ushakov and T. F. Vlasova [1, 2]. The data on levels of blood plasma amino acids are indicative of normal renal and liver function.

Preflight total essential amino acid (EA) content was rather similar in both cosmonauts and differed little from the value we calculated on the basis of data listed in BME, but somewhat higher than according to Muller (Table 2).

Total nonessential amino acid (NA) content was higher in the CDR. In both cosmonauts, this parameter was lower than in BME and according to Muller [9, 10]. For this reason, it is not surprising that overall amino acids (EA + NA) were lower in both crewmembers than in the cited manuals. In both cosmonauts, the EA/NA ratio had a higher absolute value due to relatively greater amount of EA in plasma (see Table 2).

Tests on the 1st day after the 175-day mission revealed a decline in both cosmonauts' blood plasma levels of both of the 17 free amino acids, as compared to preflight status. The CDR showed increase only in concentration of alanine (by 10.5%), while the FLE did so for valine (by 11.1%) and histidine (by 37.5%). Moreover, glycine content showed virtually no change in the FLE. The changes in concentrations of all amino acids exceeded the margin of error in assaying them, which is $\pm 2\%$. The plasma amino acid levels are indicative of satisfactory function of the kidneys and liver.

Among the EA in the CDR, the greatest decline was referable to concentrations of methionine, leucine, isoleucine, phenylalanine and lysine, and among the NA--aspartic acid, tyrosine, serine, proline, arginine, glycine, histidine and cystine (see Table 1).

In the FLE, among the EA there was greatest decline in concentrations of threonine, lysine, isoleucine, phenylalanine and methionine, and among the NA--proline, serine, alanine, glutamic and aspartic acids, tyrosin and, to a lesser extent, arginine and cystine (see Table 1).

There was a decrease in concentration of only lysine in both cosmonauts to a similar extent in mg% and as a percentage. Although the changes in other amino acids did occur in the same direction, in the direction of decline in concentration, they differed appreciably in the CDR and FLE in terms of mg% and percentage of preflight base level. After the mission, both cosmonauts presented a decrease in total amino acids (EA + NA) to about the same extent (see Table 2). There was slightly greater decrease in total EA for the CDR and NA for the FLE. There was insignificant change in EA/NA ratio in the CDR and none in the FLE. These parameters confirm the reduction in pool of free amino acids in cosmonauts' plasma in the postflight period, and to about

the same extent in both cosmonauts. Decreased intake of amino acids with food, particularly since the inflight daily food allowance was known to contain fewer amino acids than the allowance during preflight training, when daily expenditure of energy and basic nutrient requirements were higher, could be one of the causes of decrease in spectrum of free amino acids in blood plasma.

According to the approximate data in BME [9], on the first postflight day the plasma levels of lysine, threonine, valine, alanine, glycine, glutamic acid and proline remained in the physiological range for healthy adults. However, the concentrations of most of them were below the mean values and close to the bottom of the normal range. Only threonine and alanine exceeded the mean of the physiological range for adults. Against the background of decrease in concentrations of the other amino acids, alanine content increased in the CDR, but rather insignificantly. In the FLE, alanine content in plasma decreased by 33.8% and was lower than the mean of the normal range. In the CDR, methionine, leucine, isoleucine, cystine, tyrosine, arginine, aspartic acid, histidine and serine levels in plasma were below the bottom of the physiological range for these amino acids [9]. Before the flight, in the CDR the levels of only three of the above-mentioned amino acids (methionine, cystine and aspartic acid) were below the indicated norm. As compared to the preflight amino acid status of the CDR, postflight there was even greater decrease in concentrations of these amino acids: methionine to 0.10 mg% (or by 65.5%), cystine to 0.63 mg% (or by 19%), aspartic acid to 0.86 mg% (or by 34%). There was also a decline of summary indicators of plasma amino acid content. Total amino acids (EA + NA), which characterize the quantitative aspect of the blood plasma amino acid pool, decreased to 7.57 mg% (or by 28%) in the CDR, and drew close to the bottom of the range of physiological fluctuations of this parameter [9]. Total EA and NA also diminished (see Table 2) and came close to the bottom of the normal range. EA/NA changed to a lesser extent, by only 7.8%, but, as was the case preflight, it remained appreciably higher than cited in [9]. When compared to the data of Muller [10], in the CDR postflight lysine, threonine, valine, isoleucine, alanine, arginine, aspartic acid, glycine, proline, serine and glutamic acid remained in the physiological range, but the concentrations of arginine and glycine decreased to the bottom of the range. As was the case before the flight, glutamic acid content exceeded somewhat the top of the normal range, although postflight concentration decreased by 16.4%. Although alanine content did increase, it did not exceed the top limit of normal range. Most of the above-mentioned amino acids had concentrations that were below the averages cited by Muller. Postflight concentrations of methionine, leucine, phenylalanine, cystine, tyrosine and histidine were below the bottom range of physiological fluctuations according to Muller [10]. Only the concentration of cystine was below normal before the flight. Plasma levels of leucine, tyrosine and glutamic acid even exceeded the norm before the flight. The summary indicators, EA+NA, EA, EA/NA for the CDR remained in the physiological range after the flight, but came close to the bottom of the range.

Immediately after the flight, blood plasma lysine, valine, leucine, isoleucine, phenylalanine, histidine, alanine, glycine, glutamic acid and proline levels remained in the physiological range according to [9] for the FLE. However, there was a decrease in their content, with the exception of valine and histidine. Most were present in concentrations below the mean of the normal range. Threonine, methionine, cystine, tyrosine, arginine, aspartic acid and serine

were below normal. Postflight, only the concentrations of methionine, cystine, arginine and aspartic acid were below the bottom of the normal range [9]. The levels of these amino acids in plasma dropped even more during the flight. The FLE showed a decline of summary indicators: total amino acids (EA+NA) decreased by 7.26 mg% (or 28.8%), total EA by 3.21 mg% (or 28.5%) and total NA by 4 mg% (or 19%). The EA/NA ratio did not change. Parameters (EA+NA) and EA came close to the bottom of the normal range, while total NA dropped even below the bottom for this parameter. Preflight and postflight EA/NA values were higher than should be according to [9]. As compared to the Muller norm [10], we can conclude that, in the FLE, blood plasma lysine, leucine, isoleucine, phenylalanine, aspartic acid, histidine, glycine, glutamic acid and serine were in the range of physiological fluctuations immediately after the flight, in spite of the decrease in concentrations of most amino acids. Although valine and histidine content did show a postflight increase, they did remain in the normal range. The concentrations of most amino acids were lower than the means in the physiological range. Valine, glutamic and aspartic acids were an exception. The postflight concentration of threonine, methionine, cystine, tyrosine, alanine, arginine and proline was lower than the parameters cited by Muller as the bottom of the normal range. Before the flight, only cystine and histidine levels were below the bottom of the physiological range according to [10]. The summary indicators of plasma amino acid content--total (EA+NA), total EA and total NA--decreased in the FLE and came close to the bottom of the range of physiological fluctuations. Postflight EA/NA did not change. As before the flight, this ratio exceeded the top of the normal range according to Muller.

Table 3. Difference in amino acid content (mg%) in blood plasma of cosmonauts before and after 175-day flight aboard Salyut-6

| Amino acids | Preflight | | | 1st postflight d | | | 7th postflight d | | |
|---------------|---------------|------|-----------|------------------|------|-----------|------------------|------|-----------|
| | concentration | | diff. mg% | concentration | | diff. mg% | concentration | | diff. mg% |
| | CDR | FLE | | CDR | FLE | | CDR | FLE | |
| Lysine | 2.76 | 3.42 | 0.66 | 1.69 | 2.21 | 0.52 | 2.19 | 1.98 | 0.21 |
| Threonine | 2.98 | 2.48 | 0.50 | 2.45 | 0.91 | 1.54 | 3.67 | 2.23 | 1.44 |
| Valine | 2.02 | 1.98 | 0.04 | 1.91 | 2.20 | 0.29 | 1.99 | 1.72 | 0.27 |
| Methionine | 0.29 | 0.27 | 0.02 | 0.10 | 0.22 | 0.12 | 0.37 | 0.31 | 0.06 |
| Leucine | 1.82 | 1.38 | 0.44 | 0.91 | 1.26 | 0.35 | 1.33 | 1.09 | 0.24 |
| Isoleucine | 0.97 | 0.87 | 0.10 | 0.49 | 0.57 | 0.43 | 0.96 | 0.54 | 0.42 |
| Phenylalanine | 0.94 | 0.84 | 0.10 | 0.53 | 0.66 | 0.13 | 0.80 | 0.63 | 0.17 |
| Cystine | 0.78 | 0.74 | 0.04 | 0.63 | 0.70 | 0.07 | 0.68 | 0.32 | 0.36 |
| Tyrosine | 1.19 | 0.72 | 0.47 | 0.57 | 0.56 | 0.01 | 0.99 | 0.83 | 0.16 |
| Alanine | 3.12 | 3.19 | 0.07 | 3.45 | 2.11 | 1.34 | 3.32 | 3.59 | 0.27 |
| Arginine | 1.32 | 0.96 | 0.36 | 0.86 | 0.84 | 0.02 | 1.13 | 1.02 | 0.11 |
| Aspartic acid | 0.22 | 0.27 | 0.05 | 0.09 | 0.21 | 0.12 | 0.13 | 0.14 | 0.01 |
| Histidine | 1.02 | 0.88 | 0.14 | 0.72 | 1.11 | 0.39 | 0.89 | 0.87 | 0.02 |
| Glycine | 1.66 | 1.21 | 0.45 | 1.08 | 1.21 | 0.13 | 1.02 | 1.20 | 0.18 |
| Glutamic acid | 2.13 | 2.04 | 0.09 | 1.78 | 1.44 | 0.34 | 1.69 | 3.05 | 1.36 |
| Proline | 2.15 | 2.48 | 0.33 | 1.38 | 0.86 | 0.52 | 1.76 | 1.39 | 0.37 |
| Serine | 1.66 | 1.49 | 0.17 | 0.82 | 0.88 | 0.06 | 1.68 | 0.78 | 0.90 |

During this long-term mission, both cosmonauts were in virtually the same environment and on the same diet, and it would seem that this should have led to substantial equalization of amino acid concentrations in blood plasma, as compared to the base status. However, according to the data listed in Table 3, this assumption turned out to be true only for a small part of amino acids. Immediately after the flight, the difference in plasma concentration of amino acids between the CDR and FLE decreased for only 6 out of the 17 free amino acids (lysine, leucine, tyrosine, arginine, glycine and serine), as compared to preflight status. It increased for the rest of the amino acids. While the changes in most amino acids of plasma were all in the direction of decline, at the time of the postflight test the concentrations differed in absolute and percentile expressions. Consequently, the substantial equalization of living conditions and diet during the long-term flight was associated with equalization of concentrations of only some free amino acids of plasma. This phenomenon could be due to prevalence of the influence of the set of individual metabolic distinctions (including those referable to protein and amino acid metabolism) over the influence of the homogeneous set of environmental and nutritional factors. On the other hand, the fact that the actual food intake was not entirely identical during the flight, that there was a dissimilar load when performing physical exercises and various daily energy expenditures, individual endurance of flight factors and dissimilar relationship between anabolic and catabolic processes in the body could have been of some relevance.

On the 7th postflight day, the difference in amino acid concentrations continued to decline only for lysine and leucine, whereas it continued to increase for phenylalanine, cystine and glutamic acid. The difference in levels of some amino acids, which increased during the flight, then decreased but was still greater than in the preflight period. None of the amino acids returned to the difference in concentration present in the base period. Evidently, this is attributable to a different combination of living conditions, diet and individual state of metabolism, including amino acid metabolism.

By the 7th postflight day, levels of most amino acids in plasma rose in the CDR, as compared to the status on the 1st postflight day. Alanine and glutamic acid were an exception, but the subsequent decline therein was insignificant, so that their concentrations remained at virtually the same level. Total amino acids, total EA and total NA also increased, as compared to the immediate postflight values. Thus, most amino acid levels changed in the direction of returning to the preflight base level, and the concentrations of threonine, methionine, isoleucine and alanine reached the initial preflight level or even exceeded it. The summary indicators of amino acids in plasma had not yet reverted to their base status.

The findings were somewhat different for the FLE on the 7th day. As compared to the 1st postflight day, there was further decrease in concentrations of lysine, valine, leucine, isoleucine, phenylalanine, cystine, aspartic acid, histidine, serine, while glycine content did not change. Threonine, methionine, tyrosine, alanine, arginine, glutamic acid and proline levels rose. Methionine, tyrosine, alanine, arginine, histidine, glycine and glutamic acid levels reached preflight levels. Summary indicators also failed to revert to the preflight base level.

Consequently, complete recovery of base levels of a significant part of blood plasma amino acids did not occur within 7 days after the flight in either cosmonaut, although there was an apparent trend toward return of the amino acid spectrum and pool of amino acids as a whole to the preflight levels. Evidently, the unique postflight dynamics of amino acids in the cosmonauts' blood plasma are attributable to both intensive anabolic processes, primarily in the muscular system in the course of readaptation to earth, and relatively inadequate intake of many amino acids with food.

These studies demonstrated a drop in levels of most of the 17 free amino acids in blood plasma after completion of a 175-day flight and partial restoration of the initial preflight pool of amino acids by the 7th day of the postflight rehabilitation period. An amino acid supplement to the food allowance could have some preventive effect during the flight and readaptation period. In this respect, methionine, leucine, isoleucine, phenylalanine, lysine, threonine, cystine, tyrosine and arginine are the best candidates as supplements to onboard diet. In the recovery period, it is desirable to add to the diet amino acids, the levels of which did not revert to the preflight value by the 7th day, first of all, lysine, threonine, valine, leucine, isoleucine, phenylalanine, as well as methionine and cystine, the levels of which were relatively lower after the flight. In addition, it is desirable to use a methionine and cystine supplement for the preflight diet.

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EVALUATION OF CHANGES IN HUMAN AXIAL SKELETAL BONE STRUCTURES DURING LONG-TERM SPACEFLIGHTS

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[Article by G. P. Stupakov, V. S. Kazeykin, A. P. Kozlovskiy and V. V. Korolev]

[English abstract from source] Changes in the mineral content of the left heel bone of the Salyut-6 crewmembers who made 75-184-day flights were measured by direct photon absorptiometry. The postflight results were compared with the predicted rate of bone atrophy. This parameter was derived from the data concerning variations in the mineral content of spongy bones of men and animals exposed to actual and simulated weightlessness for various time intervals. The efficiency of countermeasures against the adverse effect of weightlessness on bones was assessed. It is concluded that crewmembers with a high content of minerals in spongy structures of the axial skeleton and a low basal metabolism should be selected for prolonged space missions.

[Text] Real and simulated weightlessness causes development of osteoporosis of spongy structures of the static skeleton [1, 2]. The severity of bone tissue atrophy is subject to significant individual variability, both within a biological species and in the interspecific aspect [3, 4].

Our objective here was to make a quantitative evaluation of the severity of osteoporosis in various human spongy bones during long-term spaceflights, to check the methods of preflight prediction of rate of bone atrophy and assess the efficacy of means of prevention of the adverse effect of weightlessness on bone tissue.

Methods

Preflight examination of cosmonauts included assay of minerals in the calcaneus and testing of basal metabolism. Minerals were measured by direct photon absorptiometry using the Bone Scanner 7102 of the Studsvik Firm (Sweden). The calcaneus was scanned with use of the radioisotope ^{241}Am , for which purpose the tested region of the foot was immersed in a plastic pan filled with water. In all, 20 scans were made at intervals of 1.6 mm covering the region of the

calcaneal tubercle and part of its body with a constant distance of 3.2 cm from the apex of the tubercle. The obtained parameter was expressed in grams per centimeter, i.e., the quantity of minerals (according to bone hydroxyapatite) per centimeter width of the scanning beam. In addition, we measured the volume of minerals (mineralization) of the calcaneus on the basis of a previously developed method [5]. In this study, the method was modified with consideration of the assumption that the transverse section of the bone in the tested region has the shape of an ellipse. A comparison of the results to data from using the direct method of determining mineralization of heel bones taken at autopsy revealed that there was good agreement of absolute values in both instances (coefficient of correlation $r = 0.92$).

Basal metabolic rate* was determined by the conventional method of Douglas-Haldane using a Spirolit-2 instrument. On the day before the flight, the cosmonauts did not adhere to any special diet (they used the flight ration meals). Samples of exhaled air were taken immediately after they awoke in the morning, about 10-12 h after the last food intake. For comparison, we calculated nominal values for basal metabolism with consideration of data on height, weight and age from the Harris-Benedict tables.

Postflight testing was performed at different times (see Table). Preflight examination of the cosmonauts was performed at the scheduled time, with the

Results of examining crewmembers [CDR-- commander, FLE--flight engineer]

| Crew member | Spaceflight duration, days | Postflight day of testing | Change in mineral content of calcaneus, % | |
|-------------|----------------------------|---------------------------|---|-----------------|
| | | | entire flight | monthly average |
| CDR | 140 | 5 | -3.0 | -0.64 |
| FLE | 140 | 4 | -19.8 | -4.24 |
| CDR | 175 | 5 | -9.8 | -1.69 |
| FLE | 175 | 5 | -3.0 | -0.51 |
| CDR | 184 | 14 | -9.6 | -1.56 |
| FLE | 184 | 14 | -4.4 | -0.71 |
| CDR | 75 | 4 | -0.9 | -0.36 |
| FLE | 75 | 4 | -3.2 | -1.31 |

exception of the crewmembers who participated in the 140-day mission. In this case, we used long-term postflight data as the base, which were obtained after 1.5 years for the commander (CDR) and 2 years for the flight engineer (FLE).

Results and Discussion

Initial mineral content of the calcaneus was in the range of fluctuations for healthy individuals of the same age in all of the cosmonauts. The intensity of energy expenditure at rest constituted 21 to 24.7 kcal/kg/day for the crewmembers, and it was in the range of the physiological norm. The difference from nominal basal metabolism did not exceed $\pm 4.7\%$. The preflight prognosis of severity of atrophy of spongy structures of the calcaneus was made on the basis of a mathematical model of development of osteoporosis, which was developed for this purpose. To construct it, we used results taken from the literature

of experiments with subjects kept on strict bed rest for up to 20 weeks, as well as data on rate of development of osteoporosis and parameters that cause it, which we obtained in experiments with animals (rats and dogs). Rats endured

*Basal metabolic rate was tested by V. V. Shchigolev and Yu. V. Katayev.

19-22-day spaceflights aboard Cosmos series artificial earth satellites and dogs tolerated 90- and 345-day hypodynamia with elimination of support function of the thigh. In both instances, mineralization of distal epiphyses of the heads of the femurs was analyzed.

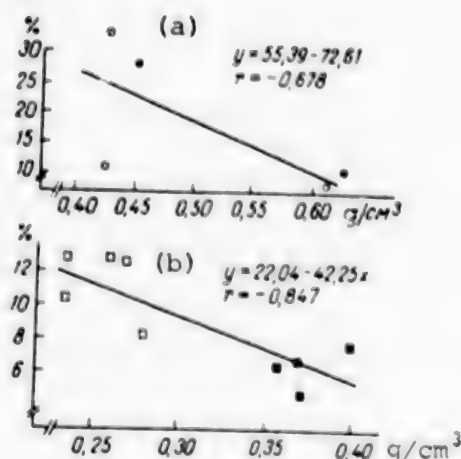


Figure 1.

Severity of dystrophy of spongy substance as a function of its initial mineralization. Dark symbols--specimens from head, white symbols--specimens from distal femoral epiphyses

a) rats b) dogs

of the intensity of basal metabolism, which ensued from the corresponding interspecific functions.

Thus, it was deemed desirable to draw a comparison between the rate of bone atrophy and index as expressed by the ratio of basal metabolism (bm) to mineralization (mn): bm/mn . This method of assessing bone atrophy underwent preliminary checking in a test on six healthy young subjects who had maintained strict bed rest for 1 month. The results of the forecast virtually coincided with the instrument test data for the calcaneus (Figure 2). Average monthly rate of development of osteoporosis in the cosmonauts' calcaneus also corresponded to the prognosis (see Figure 2).

We assessed mean monthly atrophy on the basis of preflight determination of mineralization of vertebrae and this function. This enabled us to determine the extent of postflight decrease in resistance of the spine to impact accelerations in the head-pelvis direction, with consideration of individual evaluation of parameters of traumatizing accelerations.

The conformity of predicted and observed severity of bone atrophy makes it necessary to assess the efficacy of existing methods of preventing it. One can expect these methods to be highly effective, provided a level of stress is created in the skeleton that conforms to the effect created by earth's

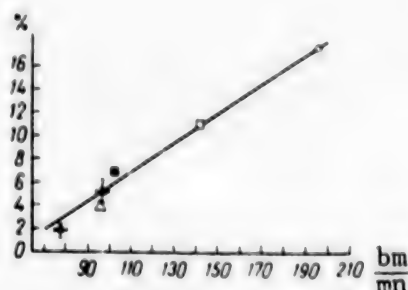


Figure 2.

Rate of bone dystrophy (%) as a function of relative index of osteoporosis (bm/mn) White triangle--man [6], black--man (hypodynamia), black circle--man (weightlessness), black and white squares--dog, white circle--rat

The model enabled us to consider the two basic theses we established: 1) relative rate of atrophy of bone tissue is an inverse function of initial mineral content of spongy bone tissue (Figure 1); 2) severity of osteoporosis is a function

gravity. The results we obtained from testing the density of spongy structures in rats submitted to constant centrifuging at an acceleration of 1 G aboard Cosmos-936 artificial earth satellite [6] serve as experimental confirmation of the possibility of preventing development of osteoporosis.

Another condition for successful use of preventive measures is the time for which they are used. It is known that spending about 1 h standing quietly and the rest of the day on bed rest did not prevent a negative calcium balance [7], whereas 3-h exposure is sufficient for a prophylactic effect [8].

Consequently, when assessing the preventive effect of physical conditioning used aboard the Salyut-6 station, it is necessary to take into consideration both of the above-mentioned conditions.

The principal ways and means of physical conditioning for cosmonauts, which create a force load on the skeleton, included exercise on a KTF [expansion unknown] stand and wearing a load [probably Penguin] suit. In assessing the adequacy of force on the spine provided by the physical conditioning measures, we considered two factors: 1) ratio of exertion to the calcaneus to that of the spine on the ground; 2) same ratio with use of physical conditioning measures in simulated weightlessness (horizontal position). Changes in the spine were assessed on the basis of these data and severity of atrophic changes in the calcaneus. To assess the significance of exercises on the KTF stand, we tested two subjects in order to determine the characteristics of transmission of impact accelerations along the body when running in vertical and horizontal position. Impact accelerations were recorded in the submalleolar region of the leg, on the level of the third lumbar vertebra (L_3), in the region of the shoulder and on the head, using the measuring complex of equipment of the Brull and Kjør Firm (Denmark): accelerometers, charge amplifiers, measuring tape recorder, digital storage unit with output on a two-coordinate Endim 620.02 (GDR) automatic recorder.

With the exception of the above-mentioned crural region, the shape of the impact acceleration pulse on all tested levels was close to semisinusoid. At the initial phase of the pulse on the leg, it formed peaks of very brief duration, so that we took as the maximum value acceleration multiplied by 0.7, with consideration of complete duration of its effect [9].

When running in both vertical and horizontal position, accelerations diminished proportionately to the distance from the sole (Figure 3). When running in horizontal position, each point of measurement corresponded to lower acceleration, with virtually parallel orientation of both functions.

To determine the magnitude of stress arising in the spine when running in horizontal position, we additionally used data from the literature [10]. The material used pertaining to results of direct pressure measurements in man in the intervertebral disks at the level of L_3 with the body in different positions and with a load on it served as the basis for constructing the magnitude of this pressure as a function of the exogenous force factor expressed in units of overload (Figure 4). In addition, Figure 4 illustrates an analogous function for the isolated spinal segment. The more abrupt increase in strain

in the spine from acceleration in man, as compared to a segment, is related to the increasing force of spinal muscle traction, counteracting the moment of inertia from eccentricity of the center of mass of the trunk.

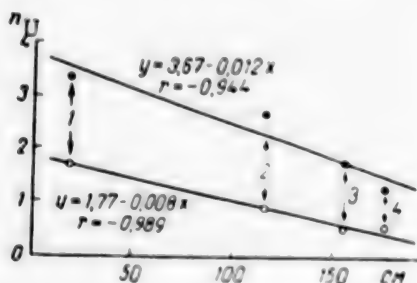


Figure 3.

Overload on the malleolus (1), lumbar region (2), arm (3) and head (4) of subject as a function of distance from support when running on KTF

Black circles--vertical position,
white--horizontal position

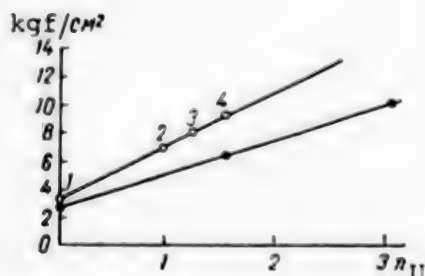


Figure 4.

Pressure in intervertebral disk of L_4 as a function of acceleration

White circles--test on man in supine position (1), standing (2), standing with 10-kg weight (3) and with 15 kg (4); black circles--tests on spinal segments with static load.

A comparison of the curves in Figures 3 and 4 indicates that strain in the spine at the time of exposure to overload when running in horizontal position is close to the strain when standing erect. Overall duration of this strain when the measured impact pulse lasts 0.12 ms, at a running rate of 180 steps/min and total time spent on the exercise of 2 h, constitutes about 45 min. On the basis of the above-mentioned data from the literature, it can be concluded that this is not enough time to completely prevent bone atrophy. If this exercise has a prophylactic effect, proceeding from similarity of the gradient of transmission of overload along the body in vertical and horizontal position, the ratio of severity of atrophy of calcaneal bone tissue to that of the spine should correspond to the ratio observed without use of preventive measures.

In evaluating the efficacy of the load suit, we proceeded from the premise that it is possible to increase tension in the spine, not only because of the force effect of elastic elements of the suit, but active muscle tone as a response to possible appearance of flexing moment in the trunk. To check this, we conducted studies, in which we applied a load of 20 kgf to the trunk of subjects in horizontal position on their side, using elastic traction devices secured on the belt. This did not

lead to increase in spinal muscle tone and, consequently, to additional increase in tension in the spine. A weight of 20 kgf was used as the maximum possible one for long-term wearing of the load suit [11].

The differences in rate of atrophic changes in the group of cosmonauts and subjects enable us to conclude that it is desirable to screen individuals for long-term missions on the basis of the criterion of high mineralization and low basal metabolism. This is motivated by at least two important factors: 1) such individuals have a spine with greatest resistance to impact accelerations; 2) the rate of atrophic changes in the skeletal bones in weightlessness

will be minimal in them. Perhaps, in such cases development of osteoporosis stabilizes without reaching any marked degree.

The above data are indicative of the need to continue research to improve the efficacy of means of preventing bone atrophy during long-term spaceflights.

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STUDY OF ERYTHROCYTE ADHESION IN COSMONAUTS

Moscow KOSMICHESKAYA BIOLOGIYA I AVIAKOSMICHESKAYA MEDITSINA in Russian Vol 18, No 2, Mar-Apr 84 (manuscript received 20 Jan 83) pp 38-40

[Article by A. A. Lentsner, V. I. Brilis, T. A. Brilene, Kh. P. Lentsner, V. M. Shilov, N. N. Liz'ko, G. D. Syrykh and V. I. Legen'kov]

[English abstract from source] The adhesive property of red blood cells of cosmonauts was investigated during various stages of their professional activity. The study was carried out using three test microorganisms: *L. casei* A6, *L. brevis* A16 and *L. buchneri* A14. The results show that the adhesive property of red blood cells varies during different periods of spaceflight. In contrast to long-duration flights, short-term flights cause greater changes in this parameter. During readaptation the adhesion of red blood cells was significantly increased as compared to that preflight and immediately postflight.

[Text] In recent years, increasing attention is being given to adhesion of microorganisms to different macroorganism cells, since the first phase of an infectious process often depends on it, as well as composition, stability and protective properties of microflora [1-3]. This matter has not been investigated from the standpoint of aerospace medicine.

Erythrocytes are the most accessible of macroorganism cells for studying adhesion. Erythrocytes are similar to other cells of the human body in many structural components (first of all, in antigenic composition). During spaceflights, there may be both quantitative [4] and morphofunctional [5] changes in red blood cells. The latter type of changes also occurred in cells of the rat's gastrointestinal mucosa during flights aboard Cosmos-782 and Cosmos-936 biosatellites [6]. As to microorganisms for the study of macroorganism cell adhesiveness, one should use bacteria encountered in the resident microflora that are in close association with mucosal epithelial cells. These microorganisms, which play a substantial part in providing for the protective function of the microflora, include lactobacilli [7, 8].

Our objective here was to investigate adhesiveness of red blood cells at different periods of professional activity of cosmonauts. We tested erythrocytes taken from crewmembers during the period of preparations for flights, the phase following their completion and in the rehabilitation period. The individuals tested including crewmembers of two prime missions (PM) of the

Salyut-6 orbital station, who participated in long-duration 185- and 75-day flights, the crews of 4 rendezvous missions (RM) to Salyut-6 aboard Soyuz-36, Soyuz T-2, Soyuz-38 and Soyuz-40 spacecraft, as well as individuals who had undergone training with the former prior to the missions. In all we examined 23 cosmonauts. The microorganisms we used were lactobacilli.

Methods

Blood was drawn from the ulnar vein into test tubes with heparin. Medium 199 was used to preserve the red blood cells.

We studied erythrocyte adhesiveness using 3 test microorganisms, *Lactobacillus casei* A6, *L. brevis* A16 and *L. buchneri* A14, which had been selected in the course of preliminary tests out of 37 strains of lactobacilli. The results of the tests were expressed as the indicator of erythrocyte adhesiveness (IEA), which is the mean index of adhesiveness of the 3 test microbes established for the studied red blood cells. The index of microorganism adhesiveness (IMA) is the mean quantity of bacterial cells per erythrocyte participating in the adhesion process. The method we used to study adhesion was developed in the Department of Microbiology of Tartu University [9, 10]. Variation of test results did not exceed 10%.

Results and Discussion

The obtained data are indicative of individual distinctions in red blood cell adhesiveness in the tested cosmonauts during the period of preflight training. For example, for the scientist cosmonaut who participated in the Soyuz-40 RM, IEA constituted 2.95 and for the scientist cosmonaut on the Soyuz-36 RM it was 6.85 (see Table). Substantial individual differences in IEA were also observed in the individuals who underwent training with the crewmembers before the missions.

IEA was retested during training for different missions in three cosmonauts. No appreciable differences were demonstrated between the two tests. This is indicative of adequate stability of individual distinctions in adhesiveness of microorganism cells.

There were significant postflight changes in IEA in 7 out of 10 subjects: 4 presented an increase in this indicator and 3 a decrease. There was elevation in the commanders of Soyuz-38 (from 3.24 to 5.39) and Soyuz-40 (from 3.04 to 5.49), as well as scientist cosmonauts aboard Soyuz-40 (from 2.95 to 4.49) and Soyuz-38 (from 4.36 to 5.24); there were declines in the commander of Soyuz T-2 (from 4.10 to 3.06), the flight engineer of Soyuz T-2 (from 4.27 to 3.72) and scientist cosmonaut aboard Soyuz-36 (from 6.86 to 3.14). Postflight IEA data differed little from those of the preflight period in participants of the 75-day mission. Yet, significant changes had usually been demonstrated in IEA following short-term flights. The participants in the 185-day mission were not examined in the preflight period. However, their postflight indicators were similar to those of the crew of the 75-day mission. Postflight IEA was elevated in the commanders of Soyuz-36, Soyuz-38 and Soyuz-40, whereas it was low in the commander of Soyuz T-2. All of the scientist cosmonauts presented significant fluctuations of IEA.

Cosmonauts' IEA at different periods of professional activity

| Crew | Cosmonaut | IEA | | |
|---------------------------------|-----------|-----------|------|-----------------|
| | | preflight | L+0 | recovery period |
| Salyut-6 PM (185-day flight) | CDR | | 2.89 | 4.32 |
| | FLE | | 2.95 | 3.64 |
| Soyuz-36 RM (7-day flight) | CDR | 5.12 | 5.65 | |
| | FLE | 6.86 | 3.14 | |
| | 1st PTI | 5.02 | | |
| | 2d PTI | 6.09 | | |
| Soyuz T-4 RM (4-day flight) | CDR | 4.10 | 3.06 | |
| | FLE | 4.27 | 3.72 | |
| Soyuz-38 RM (8-day flight) | 1st PTI | 2.68 | | |
| | 2d PTI | 3.88 | | |
| | CDR | 3.24 | 5.39 | |
| | FLE | 4.36 | 5.24 | |
| Salyut-6 PM (75-day flight) | 1st PTI | 3.65 | | |
| | 2d PTI | 4.25 | | |
| | CDR | 3.31 | 2.71 | 4.23 |
| | FLE | 2.70 | 2.97 | 4.81 |
| Soyuz-40 RM (8-day flight) | 1st PTI | 3.65 | | |
| | 2d " | 3.64 | | |
| | 3d " | 3.15 | | |
| | 4th " | 3.12 | | |
| | CDR | 3.04 | 4.59 | |
| | FLE | 2.95 | 4.49 | |
| | 1st PTI | 3.28 | | |

Key:

- CDR) commander
- FLE) flight engineer
- SC) scientist cosmonaut
- PTI) individual who underwent preflight training together with crewmembers

Increased adhesiveness of macroorganism cells are instrumental in fixation of foreign microorganisms on them under conditions of impaired function of the ecological barrier formed by representatives of resident microflora. As for decrease in adhesiveness of cells, it is instrumental in disintegration of this barrier.

According to data in the literature, short-term flights, unlike those of long duration, do not lead to significant changes in morphological and functional state of red blood cells [5] or enterocytes [6]. According to our data, there is more marked change in IEA in the case of short-term flights.

The question of nature of the demonstrated changes remains open. Perhaps the described variants of IEA changes reflect differences in reactions of the human

As a result of this study, it was established that all 4 participants in the 185- and 75-day missions presented significantly elevated IEA in the recovery period, as compared to data obtained immediately after landing [L+0]. For example, this parameter rose from 2.89 to 4.32 in the commander of the 185-day mission and from 2.95 to 3.64 in the flight engineer. The corresponding indicators for the commander of the 75-day mission were 2.71 and 4.23, for the flight engineer they were 2.97 and 4.81. Studies of IEA in participants of 75-day flight established that this indicator was higher in the recovery period than in the preflight training period.

Thus, at different periods of professional activity of cosmonauts there are specific changes in IEA. As we know, the professional activities of cosmonauts are associated with changes in microflora of the digestive tract [11, 12], in particular its lactoflora [13, 14].

The findings indicate that spaceflights can lead to both increase and decrease in macroorganism cell adhesion. Significant changes in IEA in either direction apparently present a danger to man, since favorable conditions are created for development of infections.

body to emotional stress. The adaptive mechanisms that are triggered in the course of a long-duration spaceflight probably pertain to adhesiveness of body cells. In favor of this assumption is the fact that the changes in IEA were considerably less marked after long-duration flights than short-term ones.

In conclusion, it should be stressed that the demonstrated changes in adhesiveness of macroorganism cells, which present a potential danger of development of endogenous and exogenous infections, are indicative of the urgent need for an individualized approach to use of eubiotics in all stages of professional activities of cosmonauts, regardless of flight duration.

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SANITARY AND HYGIENIC FEATURES OF CABIN ENVIRONMENT IN SALYUT-7 ORBITAL STATION

Moscow KOSMICHESKAYA BIOLOGIYA I AVIAKOSMICHESKAYA MEDITSINA in Russian Vol 18, No 2, Mar-Apr 84 (manuscript received 3 Jun 83) pp 40-43

[Article by S. N. Zaloguyev, V. P. Savina, L. N. Mukhamediyeva, Yu. G. Nefedov, A. N. Viktorov, M. A. Vytchikova and T. V. Batenchuk-Tusko]

[English abstract from source] The Salyut-7 cabin environment was investigated with respect to the chemical, biological and physical factors. The gas composition was measured qualitatively and quantitatively. This determination showed a higher content of acetone and acetaldehyde when the cosmonauts worked on various trainers and unloaded the Progress cargo vehicles. The time-course study of the toxic impurities indicated that the increase in their content was transient (no more than 4 h). The microbial content was lower than in the Salyut-6 cabin environment. The study did not show a correlation between the microbial content in the environment and the time the prime crew remained onboard. There was a correlation between the microbial content, temperature variations, and conduct of certain experiments. On the whole, the Salyut-7 cabin environment was normal for the life and work of the crewmembers.

[Text] Physiological and hygienic validation of recommendations to optimize the environment of orbital stations (OS) during long-duration spaceflights involves special scientific research dealing with the distinctions of formation of the environment with regard to physical, chemical and biological factors. The parameters of the air environment (microclimate, gas composition, bacterial contamination of the air environment) had been monitored previously; however, during the time that the first prime crew spent aboard Salyut-7 OS, priority was given to sanitary and hygienic studies, which made it possible to conduct scientific studies on a broader scale, for the purpose of elaborating a future combined program for setting standards for environmental factors. The following was done for this purpose:

Sanitary and chemical evaluation of OS gas environment with respect to composition of toxic trace impurities in the course of a 24-h period as related to nature of activities of cosmonauts.

Evaluation of bacterial contamination of manned cabin of the Salyut-7 OS as an integral indicator characterizing the efficiency of operation of the life-support system (LSS), as well as efficacy of sanitary and hygienic measures implemented during work of the first prime crew and rendezvous crews.

Investigation of distinctions referable to man's heat exchange with the environment in weightlessness.

Methods

Samples were taken for sanitary and chemical analysis using a previously developed method [1]. It was planned to periodically check the levels of toxic chemical impurities in the OS gas atmosphere, as well as to study the composition of these impurities at different times (on specific work days, every 4 h) depending on the nature of the cosmonauts' activities.

The samples were taken 2 days before the crewmembers of the prime mission (PM) and rendezvous crews finished working in the OS; they were delivered to earth and analyzed under laboratory conditions using standard techniques. In order to study processes of exchange of microorganisms between crewmembers during spaceflight, the isolated cultures of pathogenic staphylococcus, *Staph. aureus*, were submitted to phage typing followed by determination of their toxic activity.

Information about the heat sensations of the cosmonauts was recorded from the results of periodic reports of crewmembers during routine communications with on-duty group leaders. The data pertaining to parameters of microclimate (air temperature and humidity, total pressure, partial oxygen and carbon dioxide pressure) were transmitted to earth from the measuring equipment of the OS.

Results and Discussion

The sanitary and chemical situation in the habitable modules of the Salyut-6 OS was good during the time spent in them by all crews. Analysis of air samples resulted in identification and quantitative assay of 22 organic substances of the following classes: ketones, aldehydes, alcohols, esters, aromatic and aliphatic hydrocarbons.

Analysis of air samples delivered from the OS enabled us to demonstrate some increase in concentrations of acetone and acetaldehyde. Fluctuations in levels of the above-listed toxic trace impurities had also been observed in the gas atmosphere of the Salyut-6 OS. Analysis of the dynamics of contamination of the gas environment over a 24-h period as related to activities of the cosmonauts revealed that the increase in amounts of acetone and acetaldehyde was transient (lasting no more than 4 h), coinciding with the time that the cosmonauts exercised on the athletic equipment and periods of unloading the Progress cargo craft.

Bacterial contamination of the station's air environment was examined twice during the period of work done by PM-1. After the first 3 months of the mission (105 days), microorganism content of air did not exceed 450 cells/m³. The

microflora was represented by epidermal staphylococcus and corynebacteria, which are constant commensals of the mucosa of the upper respiratory tract and human integumen.

Microbial contamination of the air atmosphere increased somewhat on the last day of the crew's work, and this could apparently be related to their active work to prepare for terminating work on the station. No pathogenic microorganisms or spores of mold fungi were demonstrated in the air samples. Total microorganism content of the tested parts of the interior and equipment changed over a wide range.

In addition to commensals of the human integument, spores of mold fungi, *E. coli* and pathogenic staphylococci (*Staph. aureus*), phage type 3C/55/71, which were characterized by low toxigenic activity. Identical *Staph. aureus* cultures were isolated from samples taken of the mucosa of the upper respiratory tract of flight engineers of the prime mission and rendezvous crew.

During the time spent aboard Salyut-7 OS by the first prime mission crew, the microclimate parameters were within the range of comfortable values for man's ordinary habitat (see Table).

Mean values of microclimate parameters during performance of some operations aboard the Salyut-7 OS

| Operation | Air temperature, °C | | Air humidity, % | Gas composition of atmosphere, mm Hg | |
|--|---------------------|-------------|-----------------|--------------------------------------|-----------------|
| | mean | range | | O ₂ | CO ₂ |
| Technological experiments | 23,9 | 23,0 - 25,6 | 40 - 60 | 160-188,1 | 1,76-5,60 |
| Television broadcasts | 23,3 | 22,0 - 24,7 | 40 - 70 | 159-198 | 1,2-5,90 |
| Visit by rendezvous crew | 23,7 | 23,0 - 25,5 | 50 - 60 | 156-183 | 3,7-5,7 |
| Mean parameters during period of first prime mission | 21,8 | 17,0 - 25,6 | 40 - 80 | 152-200 | 0,5-6,0 |

At the same time, when conducting studies to set standards for microclimate in flight vehicles, with consideration of the specifics of man's work at this stage, it was deemed necessary to determine the range of temperature and humidity preferences of cosmonauts. A comparative analysis of temperature sensations of crewmembers of Salyut-7 and Salyut-6 OS and parameters of microclimate revealed that uncomfortable temperature sensations, defined by the concepts of "cold" and "cool," which were indicative of moderate strain on heat regulation [2-4], were observed in all subjects at air temperatures below 19°C and relative humidity over 60%. Sensations of "good" and "comfortable" usually corresponded to ambient temperature of 22-24°C. Consequently, according to the temperature sensations of cosmonauts, the air temperature range of 19 to 24°C can be considered the range of permissible fluctuations acceptable for man under OS conditions. However, since

setting standards for indoor ambient temperature involves determination of the zone of thermal comfort that provides for physiological rest of the heat-regulating system in 80% of the people, it can be assumed that experimental studies to pinpoint the comfort zone should be conducted in the temperature range of 22 to 24°C. Higher values for the range of thermal comfort in a spacecraft cabin, as compared to man's ordinary living conditions, are consistent with the general tendency toward perception of optimum air temperature in confined quarters [4, 5].

Perception of ambient temperature is attributable, to some extent, to the distinctions of peripheral circulation of man in weightlessness, which affects heat transfer processes. Optimization of the OS environment involves combined setting of environmental factors affecting man's thermal status: air temperature, humidity and velocity.

Investigation of air movement aboard Salyut-7 OS with concurrent analysis of the gas atmosphere for oxygen and carbon dioxide levels revealed that there is nonuniform distribution of air currents in different zones (from 0.00 to 0.32 m/s). It should be noted that minimal movement of air was found in the region of both sleeping places, which could elicit in cosmonauts the subjective sensation of poor ventilation.

Oxygen and carbon dioxide content in the tested zones during the period of sleep was in the range of the standards, fluctuating from 168 to 172 and from 3.0 to 3.5 mm Hg, respectively. Consequently, the uncomfortable feeling of "suffocating" reported by cosmonauts in the region of the sleeping places was due to slow air movement and not by composition of the air atmosphere with regard to levels of carbon dioxide and oxygen.

Technological experiments, performance of which is associated with appearance of additional heat sources (heating panels) may make some contribution to formation of thermal properties of the OS environment. For example, during performance of several technological experiments and television broadcasts, air temperature was 2-3°C higher than the daily mean without, however, exceeding the top limit of the neutral temperature zone. A drop in air temperature to the usual mean daily level was observed 3-4 h after terminating work with the unit. Analogous findings were made when the number of crewmembers was increased (see Table).

Thus, analysis of significance of different factors to formation of the environment in Salyut-7 revealed a correlation between some changes in temperature and performance of several technological experiments, uneven distribution of air flow and presence of zones with low circulation of air. Microorganism content in the air environment of Salyut-7 OS held at a lower level than during the period of operating Salyut-6 OS. No correlation was demonstrated between level of microbial contamination of the environment and duration of work done by the prime mission crews. These results show convincingly that in optimizing the OS environment it is necessary to take into consideration a set of existing factors, which together could alter man's adaptation capabilities.

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DYNAMICS OF CHANGES IN METABOLIC AND ENDOCRINE PROCESSES IN HELICOPTER CREWS
DURING COMMERCIAL FLIGHTS

Moscow KOSMICHESKAYA BIOLOGIYA I AVIAKOSMICHESKAYA MEDITSINA in Russian Vol 18,
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[Article by I. M. Nosova, T. A. Drobyshevskaya and N. A. Osadchiyeva]

[English abstract from source] Metabolic and hormonal variations of crewmembers of MI-6 and MI-8 helicopters were investigated. The investigation was performed on 61 pilots, including 18 in the hot and 43 in the cold climate. The following parameters were measured before and after flight: nonesterified fatty acids, lactic acid, insulin, and cortisol in blood, and catecholamines and cortisol in urine. In the hot climate the content of nonesterified fatty acids, lactic acid and insulin increased. The renal excretion of catecholamines and cortisol grew drastically. In the cold climate nonesterified fatty acids increased postflight. Insulin, catecholamines and cortisol tended to grow.

[Text] The professional activities of flight personnel in helicopters is related to prolonged exposure to a number of deleterious factors (flying distinctions, high noise and vibration levels, difficult meteorological and climate conditions, etc.), which is related to great nervous and emotional stress [1, 2] and is associated with significant alteration of mechanism of metabolic and endocrine regulation, and in some cases this could be the cause of functional impairment and decline of work capacity.

Our objective here was to study the effect of professional activities on metabolic and endocrine processes among flight personnel in the helicopter aviation, who fly in hot and cold climates.

We did not encounter similar studies in the accessible literature.

Methods

We examined 61 pilots 22-45 years of age, 18 of whom worked in a hot climate zone (Ashkhabad and Mary airports) and 43 in a cold one (Ukhta and Vorkuta airports). All of the subjects were deemed fit, allowed to fly without restrictions and performed commercial flights in the region of their residence (for at least 3 years), i.e., in the climate belts we studied.

The commercial flights were intermitten, each lasting 30 min to 1.5 h, with 10 to 60 min intervals between them.

A set of biochemical tests was performed involving assays of nonesterified fatty acids (NEFA) in blood, which constitute the energetically most significant lipid fraction of plasma [3, 4], by the method in [5], and the concentration of lactic acid (LA), which is the conventional indicator of status of redox processes, by the method in [6].

We evaluated the endocrine system by the levels of insulin and cortisol, which were assayed by a radioimmunological method. Concurrently, we assayed catecholamines (CA), epinephrine (E) and norepinephrine (NE) in urine by the method in [7]. The tests were performed 30-60 min before and 30-60 min after the flights.

Results and Discussion

As can be seen in Table 1, flight work in a hot climate was associated with a number of changes in the parameters studied: elevation of blood NEFA level (by 15.3%), increased concentration of LA (+21.2%) and drastic increase in insulin output (+187.32%). At the same time, there was a drop in blood cortisol level (by 56.1%).

Table 1. NEFA, LA, insulin and cortisol content of blood in helicopter personnel in a hot climate ($M \pm m$; $n = 16$)

| Time of tests | NEFA, meq/l | LA, mg% | Insulin, μ IU/ml | Cortisol, ng/ml |
|---------------|-------------------|-------------------|-------------------------|--------------------|
| Base level | 0.85 ± 0.035 | 37.32 ± 0.4 | 4.81 ± 0.82 | 165.63 ± 3.7 |
| After work | $0.98 \pm 0.04^*$ | $45.26 \pm 0.2^*$ | $13.82 \pm 0.72^*$ | $72.77 \pm 3.67^*$ |
| Change, % | +15.3 | +21.2 | +187.32 | -56.1 |
| After resting | | 38.8 ± 2.1 | | 92.95 ± 18.55 |

Note: Here and in Tables 2-4, * refers to $P < 0.05$.

Table 2. Excretion of CA and cortisol in urine in helicopter personnel in a hot climate

| Time of tests | Cortisol, ng/min | CA, ng/min | | E/NE |
|---------------|---------------------|-------------------|--------------------|------|
| | | E | NE | |
| Base level | 0.046 ± 0.0039 | 3.9 ± 1.13 | 13.8 ± 2.48 | 0.28 |
| After work | $0.079 \pm 0.008^*$ | $8.86 \pm 0.45^*$ | $19.91 \pm 0.92^*$ | 0.45 |
| Change, % | +71.74 | +127.0 | +44.27 | |
| After resting | | 5.01 ± 1.33 | 16.3 ± 2.9 | 0.30 |

The study of CA excretion in urine (Table 2) showed that E output increased by more than double after working; NE level in urine also rose and exceeded the base level by 44.27%, the E/NE ratio shifting in the direction of prevalence of E (0.23 before work and 0.445 after). Cortisol excretion in urine was also increased, exceeding the base level by 71.74% (see Table 2).

Studies of the tested parameters in pilots after a rest period, the duration of which was the same as flight time, enabled us to establish that blood NEFA and LA levels underwent virtually no change after the break, as compared to base levels (see Table 1), while cortisol content decreased, but to a lesser extent than after flights.

CA levels in urine did not rise after resting, E/NE remained on the same level (0.28 base level, 0.30 after break).

Thus, marked changes occurred in pilots in metabolic and endocrine processes, particularly with regard to metabolism of biogenic amines, under the influence of flight work.

The increased CA output is due to activation of the adrenosympathetic system, and it serves as the earliest and most reliable indicator of development of a stress reaction [8, 9]. The change in E/NE in the direction of rise of E characterizes development of a reaction over the hypothalamus--hypophysis--adrenal cortex axis [10].

The increased excretion of cortisol in urine is indicative of activation of glucocorticoid function of the adrenals, which is typical of the early phase of an adaptive reaction [11]. Activation of the pituitary--adrenal cortex system in stress situations has been described in the literature [12-17]. At the same time, we found that blood cortisol level was lower 30-60 min after flights (at the end of the work day).

Since it is a known fact that most biological processes (including cortisol secretion) are subject to a circadian rhythm with increased secretion in the daytime and decrease in the evening and at night, we compared blood cortisol levels in the pilots at the same time of day after flights and after rest periods.

We found that the postflight decline of cortisol level was more marked than after resting. This indicates that the decrease in cortisol is not only due to circadian rhythm, but possible consequence of the second phase of stress development, the refractory stage according to Selye [18], which precedes the depletion stage. The latter could be evaluated as an adverse sign of incipient fatigue.

The demonstrated increase in blood plasma NEFA could be interpreted as a manifestation of adaptive reaction, since the increase in total plasma NEFA per unit body mass also increases the process of their utilization in oxidative processes [19], which provides for conformity of energy production to energy requirements of the working body [20]. A change from energy metabolism of the "carbohydrate" type to the "fatty" type has been also observed by other researchers with exposure to subextreme and extreme factors [21].

Table 3. NEFA, LA, insulin and cortisol levels in blood of helicopter crews making commercial flights in cold climate

| Time of test | NEFA, meq/l | LA, mg% | Insulin, μ IU/ml | Cortisol, ng/ml |
|--------------|-----------------------------|---------------------------|---------------------------|------------------------------|
| Base level | 1.19 ± 0.09 (n=12) | 28.8 ± 0.29 (n=19) | 17.9 ± 0.44 (n=20) | 188.05 ± 1.063 (n=19) |
| After work | $1.53 \pm 0.11^*$ (n=19) | 25.7 ± 0.23 (n=19) | 19.6 ± 0.48 (n=19) | $78.06 \pm 0.42^*$ (n=20) |
| Change, % | +28.5 | — | — | -58.51 |

Table 4. CA excretion in urine of helicopter crews making commercial flights in cold climate

| Time of test | CA, ng/min | | E/NE | Cortisol, ng/min |
|--------------|-----------------------------|-----------------------------|--------|-------------------------------|
| | E | NE | | |
| Base level | 8.8 ± 0.96 (n=20) | 18.2 ± 2.6 (n=20) | 0.48 | 0.039 ± 0.004 (n=4) |
| After work | $14.2 \pm 0.27^*$ (n=43) | $23.7 \pm 0.32^*$ (n=43) | 0.599 | $0.064 \pm 0.007^*$ (n=13) |
| Change, % | +61.35 | +30.22 | +24.79 | +64.06 |

Studies conducted in a cold climate (Table 3) revealed that helicopter pilots present changes in metabolic and endocrine processes under the influence of their professional activities, mainly in the form of changes analogous to those demonstrated in the hot climate, although the extent varied. For example, blood NEFA content also increased postflight (+28.5%) and there was a tendency toward increase in insulin concentration. The decline of cortisol level constituted 58.51%.

E excretion in urine was 14.2 ng/min and NE was 23.7 ng/min. The E/NE ratio was 0.599, which exceeded the control level by 61.36, 30.22 and 24.79%, respectively (Table 4). There was concurrent increase in cortisol excretion in urine (by 64.1%).

In spite of the similar nature of noted changes, with the flights in a hot climate we observed more marked metabolic changes, as indicated by the reliable increase in LA content of blood. The increase in lactate concentration during the flight could serve as a sign of fatigue.

A comparison of dynamics of changes in the parameters studied in blood of pilots referable to the two climate zones impressed us by the reciprocity of correlations between blood LA and NEFA concentrations. Thus, while blood NEFA content in the hot climate was below the level observed in pilots at the

Extreme North, LA concentration, on the contrary, was considerably higher in pilots in the hot climate than the same parameter in pilots in other climates. The demonstrated high values for blood NEFA levels in flight personnel in the Extreme North are due to the specifics of metabolic processes inherent in that region, and they are related to acclimatization.

It is known fact that metabolism changes in the direction of prevalence of lipid metabolism, as being energy-filled material in the course of acclimatization to a cold climate [21].

Conversely, in a hot climate, there is prevalence of carbohydrate metabolism, and its distinctions are glycogen breakdown and, as a result, relatively high LA level in blood. The low base level of blood insulin that we found in pilots who made flights in a hot climate could be due to a reflex response to possible hypoglycemia, which requires strict monitoring of blood sugar in the group of subjects studied. We cannot rule out the possibility that the low base level of insulin is indicative of depletion of functional capabilities of the pancreas, which also requires monitoring of pancreatic function.

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CHOICE OF PSYCHOPHYSIOLOGICAL CRITERION TO ASSESS WHOLE-BODY LOW-FREQUENCY VIBRATION

Moscow KOSMICHESKAYA BIOLOGIYA I AVIAKOSMICHESKAYA MEDITSINA in Russian Vol 18, No 2, Mar-Apr 84 (manuscript received 24 Jan 83) pp 47-50

[Article by Yu. N. Kamenskiy]

[English abstract from source] In response to whole-body vibration of 10 Hz and acceleration of 1 m/sec^2 applied for 1 hour the psychophysiological status varies in two stages. At stage 1 physiological functions are disturbed (primary disorder) and at stage 2 they recover partially or completely (compensation and adaptation). The level of compensatory and adaptive reactions can be used as a tolerance criterion of the vibration effect with respect to its magnitude and duration. The primary reaction can be used as such a criterion when the functions under study are exposed to direct biomechanical effects of vibration.

[Text] The change in working conditions for operators of modern transport (less physical activity, increased emotional and operating tension, improved microclimate) have caused an increase in the role of vibration as a factor that causes fatigue and worsening of professional qualities of an operator. For this reason, it became necessary to select levels of vibration to which an operator is exposed in order to assess his condition and predict his professional work capacity. Apparently, such an evaluation should be based on the principle of specificity, which implies investigation of level of activity of systems that are the most responsible for operator performance, as well as the many elements of these systems and existence of functional phases in the status of man [1]. The sensorimotor functional system plays the most meaningful role in operator work. Proceeding from these theses and the results of prior studies [2], we selected several psychophysiological methods that characterize the level of activity of the sensorimotor functional system as an indicator of functional state (FS) of an operator as a whole, from the standpoint of predicting his professional reliability. Our objective was to test experimentally the significance of the chosen methods in the case of exposure to whole-body low-frequency vibration, which is the most typical of the principal means of transportation.

Methods

We conducted two series of studies: basic one, with use of vibration at a frequency of 10 Hz and acceleration of 1.0 m/s^2 , and control, without vibration but with adherence to all other conditions of the study. Sinusoid waves in a vertical direction were generated using a VEDS-200A vibration table. The parameters of vibration were checked by means of low-frequency vibroacoustic equipment conforming to GOST 13731-68. The subject sat on a hard chair. Duration of exposure was 1 h and that of aftereffects, 30 min. Ten essentially healthy men 25 to 44 years of age, whose occupation was unrelated to exposure to vibration, participated in the tests.

We used the following psychophysiological methods: flicker fusion threshold (FFT), reproduction of a given muscular exertion (RME), precision of coordinated movements (PCM) and reaction to moving object (RMO). The RMO results were evaluated according to ratio of number of premature reactions (RMO_p) to number of delayed reactions (RMO_d), which was arbitrarily called the indicator of nervous processes (INP). The subjects were examined before exposure (background), in the 1st-5th, 15th-20th, 30th-35th, 55th-60th min of exposure and 1st-5th, 15th-20th and 25th-30th min of the aftereffect period. The data were submitted to statistical processing with the condition of 95% reliability of different means.

Results and Discussion

The subjective assessment of vibration by the subjects varied. In two cases they reported a heavy feeling in the whole body, which was followed by a feeling of drastic relief right after exposure; in four cases there was a feeling of heaviness in different parts of the body (the head, legs). Four of the subjects became sleepy in the 15th-20th min of exposure. After exposure, four subjects developed a feeling of instability, which disappeared within the first minutes of the aftereffect period. Four subjects reported general fatigue; two noted vagueness of outlines of hands and digits on instruments, shaky voice, hoarseness and cough during exposure.

In the base state, the psychophysiological parameters were virtually the same in subjects of both series. During exposure to vibration, all of the parameters presented rather distinct dynamics of changes. For example, FFT decreased in 8 out of 10 subjects immediately after the start of exposure, remaining at low levels to the end of the exposure period and recovering immediately after vibration was stopped (see Table). FFT showed virtually no change in the control.

The drastic decline of FFT at the very start of exposure and complete recovery immediately after discontinuing it are indicative of the direct biomechanical effect of vibration on this parameter. The mechanism of this influence may consist of interaction between three oscillatory processes: bioelectric (cerebral cortex), photic (light flashes) and mechanical (oscillation of the head), which occurs, perhaps, on the "capture" principle [3-4]. At the same time, vibration also altered FFT in a mediated way, through changes in functional state of the body as a whole. This is indicated by the increase in fluctuation of the variation series during exposure from ± 3.6 to ± 5.4 Hz. A change

in function of the visual analyzer under the influence of vibration is a prognostically adverse sign, since this means that there is decrease in resolution capacity of the operator-instruments system and poorer perception of visual information. Consequently, a significant decline of FFT under the effect of whole-body low-frequency vibration could serve as a criterion of the influence of this factor on operators.

Dynamics of psychophysiological parameters during testing of main group of subjects, $M \pm m$

| Parameter | Back-ground | Exposure, min | | | | | Aftereffect, min | | |
|----------------------|-----------------|------------------|------------------|------------------|------------------|------------------|------------------|-----------------|-----------------|
| | | 5 | 15 | 30 | 45 | 60 | 5 | 15 | 30 |
| FFT, Hz | 32.6 \pm 1.2 | 28.1 \pm 1.2* | 27.4 \pm 1.4* | 27.1 \pm 1.5* | 26.8 \pm 1.7* | 27.9 \pm 1.8* | 31.9 \pm 1.4 | 32.6 \pm 1.5 | 32.5 \pm 1.3 |
| PCM, arbitrary units | 2.8 \pm 0.30 | 1.7 \pm 0.41* | 1.8 \pm 0.36* | 1.6 \pm 0.72* | 1.5 \pm 0.46* | 1.6 \pm 0.54* | 3.0 \pm 0.25 | 3.1 \pm 0.19 | 2.9 \pm 0.32 |
| RME, arb. units | 2.6 \pm 0.32 | 3.2 \pm 0.28 | 2.0 \pm 0.30 | 2.1 \pm 0.42 | 2.3 \pm 0.34 | 2.5 \pm 0.38 | 3.2 \pm 0.46 | 2.8 \pm 0.41 | 2.7 \pm 0.44 |
| INP, arb. units | 1.20 \pm 0.26 | 0.84 \pm 0.40* | 0.73 \pm 0.31* | 0.80 \pm 0.30* | 0.82 \pm 0.38* | 0.84 \pm 0.31* | 0.86 \pm 0.41 | 0.87 \pm 0.42 | 0.93 \pm 0.38 |

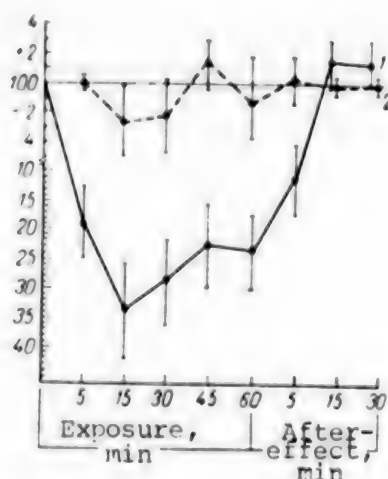
*Cases of reliable differences ($P < 0.05$) in comparison to background values.

At the start of exposure, all subjects showed drastic worsening of PCM. This parameter recovered immediately after exposure (see Table). In the control, PCM worsened somewhat in the course of the study. Apparently, worsening of PCM in the main series of subjects was due to the direct biomechanical effect of vibration, which was transmitted to the subject's hand and intensified tremor. Since the extent of transmission of low-frequency oscillations over the body is determined not only by frequency, but intensity, the PCM parameter can be used to assess the effect of vibration on an operator. A reliable decline of PCM would be a criterion of the effect.

Precision of RME at the start of exposure increased in 3 of the subjects in the main series, decreased in 4 and did not change in 3 cases. On the average, there was some increase in precision of RME (see Table). In the control series, this parameter increased in only 1 subject and did not change in 9. The cases of increased RME precision could be related to the subjects' set for good performance. A noticeable decline of RME occurred in half the subjects in the main series in the 15th min of exposure. However, by the end of the exposure period, this parameter reverted to close to the base level and in the after-effect period exceeded this level. In the control, there were insignificant fluctuations in precision of RME. Since there was a decline of RME in the 15th min of exposure, it can be assumed that vibration has an adverse effect on muscular and articular sensibility. Considering the data in the literature concerning changes in this parameter during long-term exposure to vibration [5, 6], it can be deemed desirable to use the RME method to assess the functional state of an operator. A reliable decrease in precision of RME without recovery during the exposure period would be a criterion for such assessment.

The number of accurate RMO in the course of the study changed inconsistently and insignificantly in both series of subjects. Conversely, the number of RMO_p

consistently decreased while number of RMO_d consistently increased. As a result, INP declined in both series, already at the start of the study, and recovered only at the end of the aftereffect period (see Table). The decrease in INP in this case is indicative of intensification of an inhibitory process in the central nervous system. The fact that these changes were in the same direction in the control and experimental series indicates that monotony of the test situation and relative hypodynamia of the subjects played a substantial role in intensifying the inhibitory process. However, in the main series, these changes occurred sooner (5th min of aftereffect period) than in the control (15th min of study), which is indicative of the fact that vibration plays some part in intensifying the inhibitory process, to development of sleepiness [7, 8]. Under actual working conditions, an operator is in a state of emotional and operational stress while working. All this eliminates, to some degree or other, the effects of unchanging position and monotony. There is more distinct manifestation of the inhibitory effect of vibration on an operator.



Dynamics of functional state of the subjects in the main (1) and control (2) series of tests

Vertical lines--error of mean

Use in this study of a combined evaluation of an operator's state conforms to modern views about methodology of research in industrial physiology and engineering psychology [10]. But such an approach does not provide a complete idea about the functional state of the human body. Proceeding from the experiments of other researchers [11-12], we used an integral indicator of functional state, which we called the mean percentage of change (MPC) and calculated as the algebraic sum of relative (as percentage of background values) changes in the four parameters we used, divided by their number. The dynamics of MPC in the experimental and control series were indicative of its considerably greater informativeness, as compared to special parameters (see Figure). The subjects in the main series showed a drastic decline of MPC at the start of

exposure. This initial decline can be qualified as the body's primary reaction to vibration. MPC did not recover entirely thereafter due to the high intensity of the factor used, and this is indicative of inadequate development of compensatory processes. Since there were phasic changes in the body's functional state during exposure the presence of a primary reaction or its severity cannot serve as criteria of permissibility of exposure to vibration. Recovery of MPC to close to the base level within 60 min of exposure should be considered as such a criterion, since the periodicity of changes in functional state during exposure to vibration is 50-60 min [13].

Thus, whole-body vibration at a frequency of 10 Hz and acceleration of 1 m/s^2 for 1 h elicits marked phasic changes in psychophysiological parameters characterizing the sensorimotor functional system. The first phase of functional disturbances reflects the body's primary reaction to the factor, and the second is related to development of compensatory and adaptive changes. The intensity

of both phases depends on the intensity of vibration. However, the primary reaction could be a criterion of permissibility of exposure only in the case of direct biomechanical effect of vibration on the functions studied (for example, FFT, PCM). In the case of mediated effect of vibration on some function or other, the criterion of permissibility should be an adequate degree of compensatory and adaptive reactions.

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EVALUATION OF SOME HEMODYNAMIC PARAMETERS OF PILOTS DURING FLIGHTS

Moscow KOSMICHESKAYA BIOLOGIYA I AVIAKOSMICHESKAYA MEDITSINA in Russian Vol 18, No 2, Mar-Apr 84 (manuscript received 19 Aug 82) pp 50-54

[Article by B. S. Bednenko, G. N. Grechikhin and A. N. Kozlov]

[English abstract from source] Coronary circulation and systolic and diastolic time intervals were measured in one-seat high-maneuvrability aircraft pilots during 22 flights. The effective coronary blood flow values varied significantly and reached maximum during landing. In some cases these changes were very large, suggesting a low level of conditioning and physiological reserves. It is recommended to monitor coronary circulation inflight.

[Text] It is very important to determine the state of cardiodynamics and hemodynamics of flight personnel in order to elaborate recommendations aimed at safeguarding the health of pilots, increasing reliability of their performance and flight safety [1-3]. However, during flight work (particularly in single-seat maneuverable aircraft), there is limited possibility of recording physiological parameters, which makes it difficult to obtain quantitative criteria for assessing the condition of the heart and vessels, so that one is prompted to broaden the use of informative methods [3]. Our objective here was to investigate the severity of changes in effective coronary blood flow (ECF) and phase structure of the cardiac cycle in different modes of flight aboard aircraft of the above types.

Methods

The studies were conducted during 22 flights aboard single-seat high-maneuverability aircraft with the participation of 10 pilots. They took off, performed the first segment of horizontal flight (HF-1), a maneuver, dive, second segment of horizontal flight (HF-2) and landed. We recorded the ultrasound doppler cardiogram (USDC) from the region of projection of the left ventricle (4th intercostal space on the left, near the sternum), electrocardiogram (EKG) and pneumogram (PG) using KMA-72 equipment and a loop oscillograph.

We determined the duration of cardiac (t_c) and respiratory (t_r) cycles, heart rate (HR) and respiration rate (RR) from the EKG and PG. The dynamics of

stroke ECF by means of the USDC: Q (amount of blood flowing through coronary vessels giving off oxygen to myocardial capillaries) from the integral values of signal reflected from posterior ventricular wall in systole [4-6]. We calculated the dynamics of ECF volume-- K as $K = Q \cdot f$, where f is HR change. In order to obtain comparable results, we scaled Q and K to their minimum values, which occurred prior to starting the engine in 64% of the flights and in HP-1 in the other cases. Integral values of USDC were measured by planimetry. We determined the duration of phases of the cardiac cycle: contraction (PS) and ejection (S) of blood by ventricles, protodiastole (P), relaxation (R) and rapid filling (RF) by means of USDC using a known method [7, 8], addressing ourselves to the typical signs of the signal. We calculated the following phase parameters: $M_1 = S/PS$ and $M_2 = RF/R$.

We determined at each stage of the flight coefficient M_3 , which characterizes stability of USDC recording: $M_3 = n_i/n_e$, where n_i is the number of signal complexes subject to reliable interpretation and n_e is total number of complexes.

Results and Discussion

Analysis of the results (Table 1) revealed that HR was in the range of 66-133/min in the pilots before starting up the engine, while RR was 10-48/min. In horizontal flight there were no significant changes in these parameters (according to group values). There was a reliable increase in HR during landing and take-off (by an average of 18 and 16%), while RR changed negligibly. When performing a maneuver and diving, the differences in the parameters were unreliable.

Stroke ECF in horizontal flight was higher than base value on the average, but this was unreliable. At take-off, during performance of a maneuver and dive there were significant increases in parameter Q (on the average it doubled). Its maximum increment occurred during landing (by more than 2.3 times).

The dynamics of minute ECF were somewhat more marked: K increased by more than 2 times at take-off, during maneuver and dive and by about 2.8 times at landing. The changes in minute ECF were attributable more to Q and less to HR. Since the initial HR (before starting the engine) was on the average 40% higher than at rest, it can be assumed that K was 2.8-3.9 times greater during flight than at rest.

The dynamics of the phase structure of the cardiac cycle (Table 2) were characterized by insignificant changes in PS, P, R intervals and reliable decrease in duration of S and RF. The most substantial shortening of S period was noted at landing (about 0.03 s) and for RF at take-off, landing and when diving (from 0.03 to 0.04 s). Phase parameters M_1 and M_2 were reliably diminished.

A stable analysis could be made of 67-79% of the recorded complexes.

The high HR and RR before starting the engine were attributable to the pilots' marked emotional stress during take-off. This was also confirmed by the results of phase analysis: before take-off S and RF periods were reliably shorter, while duration of S decreased by 0.04 s, as compared to the nominal values calculated using the formula of V. L. Karpman [9].

Table 1. Hemodynamic parameters of pilots during flights ($M \pm m$)

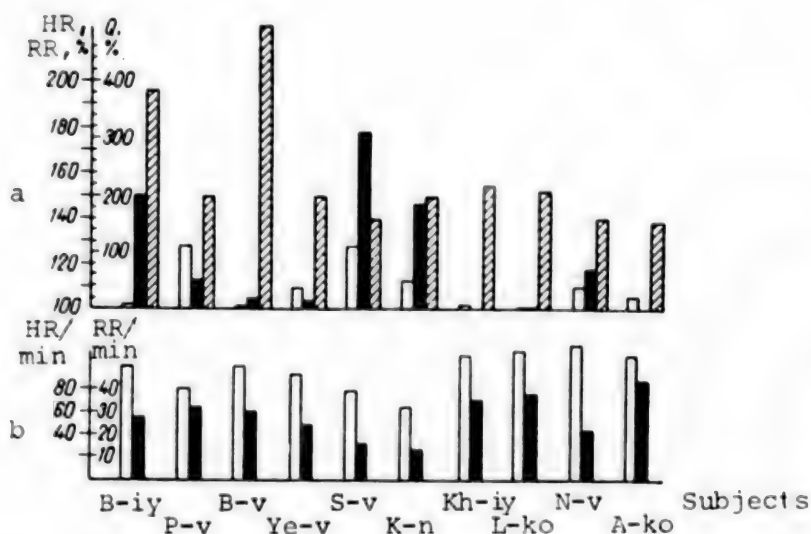
| Parameter | Before starting engine | Take-off | HF-1 | Maneuver | Dive | HF-2 | Landing |
|------------------|------------------------|------------------------|-----------------------|------------------------|-----------------------|-----------------------|------------------------|
| M ₁ P | 2.24 ± 0.10 | 1.89 ± 0.06 < 0.01 | 2.10 ± 0.10 > 0.05 | 2.13 ± 0.12 > 0.05 | 1.99 ± 0.06 < 0.05 | 1.88 ± 0.06 < 0.01 | 1.81 ± 0.06 < 0.01 |
| M ₂ P | 2.22 ± 0.04 | 1.92 ± 0.06 < 0.001 | 2.00 ± 0.08 < 0.05 | 1.88 ± 0.06 < 0.001 | 1.94 ± 0.08 < 0.01 | 2.05 ± 0.04 < 0.01 | 1.72 ± 0.04 < 0.001 |
| HR/min P | 94 ± 5 | 109 ± 5 < 0.05 | 103 ± 4 > 0.05 | 102 ± 4 > 0.05 | 104 ± 5 > 0.05 | 107 ± 9 > 0.05 | 111 ± 4 < 0.02 |
| RR/min P | 31 ± 2 | 32 ± 2 > 0.05 | 30 ± 2 > 0.05 | 29 ± 2 > 0.05 | 36 ± 2 > 0.05 | 25 ± 2 < 0.05 | 32 ± 1 > 0.05 |
| Q P | 1.08 ± 0.04 | 2.02 ± 0.16 < 0.001 | 1.19 ± 0.07 > 0.05 | 1.88 ± 0.11 < 0.001 | 1.99 ± 0.33 < 0.02 | 1.29 ± 0.20 > 0.05 | 2.34 ± 0.26 < 0.001 |
| K P | 1.08 ± 0.06 | 2.32 ± 0.17 < 0.001 | 1.30 ± 0.08 < 0.05 | 2.04 ± 0.12 < 0.001 | 2.20 ± 0.33 < 0.01 | 1.47 ± 0.21 > 0.05 | 2.76 ± 0.26 < 0.001 |

Table 2. Indicators of period structure of cardiac cycle in pilots during flights ($M \pm m$)

| Parameter | At rest (3-4 h before flight) | Before starting engine | Take-off | HF-1 | Maneuver | Dive | HF-2 | Landing |
|--------------------|-------------------------------|------------------------|--------------------------|-------------------------|-------------------------|--------------------------|-------------------------|--------------------------|
| PS, P | 0.091 ± 0.002 > 0.05 | 0.085 ± 0.002 | 0.083 ± 0.002 > 0.05 | 0.087 ± 0.002 > 0.05 | 0.087 ± 0.002 > 0.05 | 0.086 ± 0.002 > 0.05 | 0.088 ± 0.002 > 0.05 | 0.089 ± 0.002 > 0.05 |
| S, P | 0.227 ± 0.005 < 0.001 | 0.189 ± 0.006 | 0.160 ± 0.006 < 0.01 | 0.174 ± 0.003 < 0.05 | 0.169 ± 0.004 < 0.02 | 0.167 ± 0.006 < 0.02 | 0.165 ± 0.006 < 0.01 | 0.157 ± 0.003 < 0.001 |
| P, P | 0.034 ± 0.001 > 0.05 | 0.032 ± 0.002 | 0.033 ± 0.001 > 0.05 | 0.033 ± 0.002 > 0.05 | 0.034 ± 0.002 > 0.05 | 0.034 ± 0.002 > 0.05 | 0.032 ± 0.001 > 0.05 | 0.030 ± 0.001 > 0.05 |
| R, P | 0.092 ± 0.002 < 0.001 | 0.074 ± 0.002 | 0.072 ± 0.002 > 0.05 | 0.069 ± 0.002 > 0.05 | 0.077 ± 0.002 > 0.05 | 0.071 ± 0.004 > 0.05 | 0.071 ± 0.004 > 0.05 | 0.069 ± 0.001 < 0.05 |
| RF, P | 0.183 ± 0.006 < 0.05 | 0.165 ± 0.006 | 0.136 ± 0.003 < 0.001 | 0.142 ± 0.007 < 0.02 | 0.141 ± 0.005 < 0.01 | 0.136 ± 0.003 < 0.001 | 0.146 ± 0.005 < 0.05 | 0.128 ± 0.005 < 0.001 |
| t _C , P | 0.895 ± 0.028 < 0.001 | 0.637 ± 0.029 | 0.556 ± 0.19 < 0.05 | 0.580 ± 0.024 > 0.05 | 0.586 ± 0.028 > 0.05 | 0.575 ± 0.030 > 0.05 | 0.559 ± 0.047 > 0.05 | 0.540 ± 0.06 < 0.01 |
| M ₃ , % | 92 | 79 | 69 | 74 | 68 | 77 | 82 | 67 |

A comparison of the above data to results obtained for flights aboard multi-passenger aircraft revealed [8] that the changes in HR, RR and periods of the cardiac cycle were virtually identical during landings for pilots of single-seat and multiseater aircraft. Performance of horizontal flights aboard single-seaters is related to more marked circulatory system reactions and is associated with a greater load on the heart. The phase intervals (particularly diastole phases) were considerably greater for cargo pilots flying on automatic pilot than those flying in high-maneuverability aircraft.

The established changes in minute ECF and phase intervals are essentially analogous to the hemodynamic changes observed in health subjects when submitted to a high-intensity physical load [9-12]. These changes are usually related to an increase in rate of ejection of blood from the ventricles, as well as in force of myocardial contraction and rate of elevation of intraventricular pressure. However, the significant increments of stroke ECF observed in flight are not observed during physical exercise [11, 12], and they are more inherent in nervous and emotional stress [11], in the presence of which marked dilatation of coronary vessels is observed. For this reason, we believe that the increase in contractile function of the myocardium observed during flights aboard single-seat aircraft occurs against a background of active dilatation of coronary vessels, which leads to additional intensification of myocardial metabolism. The work load on the heart could triple in the presence of severe emotional stress [13].



Dynamics of recorded parameters of pilots during landing (a), as compared to base values (b). White bars--HR, black--RR, cross-hatched--Q

Consequently, as applied to the flight assignments aboard single-seat aircraft, maximum circulatory reactions occurred in pilots during landings. Significant and approximately similar hemodynamic changes were noted at take-off, during maneuvering and diving. Moderate and unreliable changes were noted in horizontal

flight. The dynamics of circulatory parameters observed inflight are typical for conditions of appreciable increase in burden on the heart.

Analysis of individual inflight circulatory reactions (see Figure) showed that they differed markedly. The changes in HR and RR depended on the level of the pretake-off reaction. In pilots with high base values for these parameters preflight (100-120 and 28-44/min), we observed minimal or moderate increase (and occasionally they remained without change). In pilots with lower base values (up to 63-80 and 17-28/min), these parameters grew.

Relative changes in stroke ECF constituted 152-200% in 8 out of 10 pilots during landings; they were substantially greater, 382 and 500%, in pilots B-iy And B-v. Such marked ECF dynamics with increase in load on the heart are typical of individuals with poor physical conditioning, who are notable for lower physiological reserves [12]. For this reason, we relate the above individual reactions to the level of pilot conditioning. This assumption was confirmed by the findings of routine medical check-ups.

Thus, we observed distinct changes in coronary circulation and phase structure of the cardiac cycle reflecting substantial intensification in contractile function and metabolism of the myocardium at several stages of flights in high-maneuverability aircraft. In some cases, the ECF increment reached high values, which apparently are inadequate to the magnitude of the flight load. It can be assumed that the presence of this type of reactions in some pilots could be instrumental in development of sudden loss of work capacity, which is encountered during flight in some cases, due to impaired cardiac function [3, 14, 15]. In order to prevent such signs, it is desirable to effect dynamic monitoring during flight work of coronary circulation, which would permit evaluation of the degree of adaptation of the cardiovascular system to loads and elaboration of individual recommendations for correcting work and rest schedules of flight personnel.

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SOME PSYCHOLOGICAL CONSEQUENCES OF PROLONGED SOCIAL ISOLATION

Moscow KOSMICHESKAYA BIOLOGIYA I AVIAKOSMICHESKAYA MEDITSINA in Russian Vol 18, No 2, Mar-Apr 84 (manuscript received 10 Jun 83) pp 54-56

[Article by J. Terelak (Polish People's Republic)]

[Text] The results of a study conducted under the environmental conditions of a stay in Antarctica [1] are of great interest from the standpoint of cosmonautics and, first of all, problems of effects on man's performance of long-term isolation related to spaceflight conditions.

In an analysis of the process of socioemotional adaptation of a small group that spent the winter in Antarctica, Strange and Klein [2] called attention to a so-called psychophysiologic price of the reaction related to this process. The behavioral disturbances demonstrated by several authors, which are due to prolonged stays in polar regions, form the so-called winterers' syndrome.

The most frequently observed manifestations of the winterers' syndrome are depression, hostility, irritability, sleep disorders, loss of interest in work, diminished intellectual capabilities and disappearance of interests.

In his critical analysis of these symptoms, Mullin [3] indicates the following possible causes of their onset: need for long-term stay in an isolated group; sameness of environment (monotony, boredom); absence of customary sources of emotional cues.

The same features had also been noted in many laboratory studies simulating spaceflight conditions.

Several authors who have described the winterers' syndrome in psychopathological [8] or psychological concepts [6] stress the nonspecific nature of the behavioral disturbances that form the syndrome. In the opinion of these authors, the observed changes lead to mental asthenization (neurasthenic manifestations gradually change into so-called polar asthenia, which is characterized by diminished interest in work and unwillingness to make any effort). According to our conceptions, this nonspecific aspect of psychological consequences of prolonged social isolation could be analyzed from the standpoint of psychophysiological or psychological conceptions which make use of the concept of optimum activity or stimulation [7-9] as the basic factor.

One of our objectives here was to try to reinterpret the well-known winterer syndrome in categories of psychological conceptions of activation (stimulation).

Methods

An extensive survey of the literature dealing with the condition of man in social isolation shows, in particular, that by virtue of intercultural differences, differences in size of wintering groups and their structural composition, as well as motivation for the tasks put to winterers, such investigations should be conducted continuously and at different polar stations [10].

For this reason, it was deemed desirable to conduct studies at the polar Antarctic station imeni Kh. Artstovskiy.

In this study, isolation is defined not only as man's separation from customary living and working conditions, but substantial limitation of his psychological space and absence of customary exogenous stimuli. This definition of isolation enables us to use data obtained under conditions of antarctic isolation for purposes of space medicine and psychology [6].

We investigated the dynamics of development of the chief symptoms making up the winterers' syndrome: processes of neurotization, introvertization, changes in daily cycle of activities, changes in affect and level of anxiety.

The subjects consisted of a group of 20 participants in a Polish Antarctic expedition (average age 34 years), who had spent 1 year in social isolation at the Artstovskiy Station (South George Island).

In order to determine the level of neurotization and extraversion, we used the Eysenck personality scale and for determination of anxiety (as a state and as a property), the Spielberger questionnaire. We used the data from self-observation (according to a specially prepared form) to study the daily cycle of activities and affect.

Results and Discussion

Figure 1 illustrates data referable to study of level of neurotization and extraversion.

As the data indicate, from the standpoint of adjustment to isolation, the first half of the wintering period was the most difficult, as indicated in particular by increase in level of neurotization (level of reliability for pairs of findings, $p \leq 0.01$) and introversion ($p \leq 0.01$ and ≤ 0.05). The demonstrated nonspecific effect of isolation in Antarctica should be interpreted from the standpoint of psychological cost of adjustment to new (with regard to stimulation) living conditions, rather than the result of gradual mental asthenization [3]. The fact that these parameters returned close to the base levels just prior to returning [home] is also indicative of the validity of such an approach.

The situational (situation of insufficient stimulation) induced progressive "withdrawal" is reflected by the results of studying four types of activity: work (solving problems put to different participants of the expedition), social work, sociability and reflectiveness. These data are illustrated in greater detail in Figure 2.

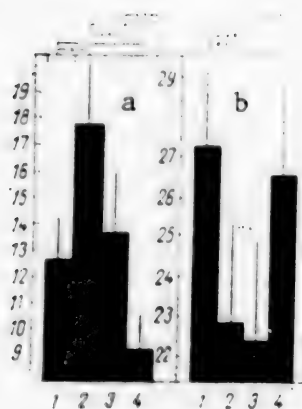


Figure 1.

Measurement of neurotization (a) and extraversion (b) using Eysenck questionnaire on winterers (1978)

- 1) before wintering
- 2-4) at start, middle and end of expedition, respectively

*) $P \leq 0.05$

**) $P \leq 0.01$

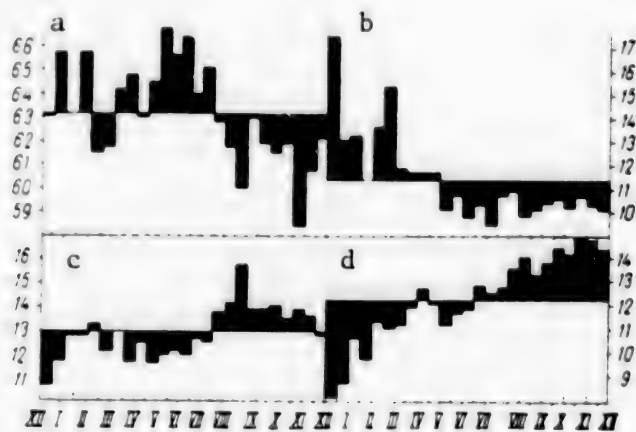


Figure 2.

Fluctuations in activity, as compared to annual mean for polar workers in isolation in Antarctica. Here and in Figures 3 and 4,* months are plotted on x-axis

a) work (annual mean 63.2)

b) social work (11.4)

c) gregariousness (13.0)

d) reflectiveness (12.3)

As shown by the results, starting in the second half of the expedition period, i.e., during the period of monotony and boredom, there were changes in the structure of activities. These findings coincide with those of other authors who noted, in particular, that in view of decrease in overall purposeful activities the winterers who had a surplus of spare time were no longer able to fulfill their personal work plans [3]. The concurrent increase in parameters of reflectiveness indicates that, in the case of inadequate exogenous stimuli, man turns to a search for sources of stimulation in his own internal activities and, in part, in other people (gregariousness [sociability]). Theoretical interpretation of the data obtained in the light of the activation conception and a more comprehensive discussion of these data are provided in [10].

The results of studying affect, in particular, are indicative of the adaptive nature of these behavioral manifestations.

The results illustrating changes in affect in 2-week cycles of observations coincide with the data obtained from the study of neurotization, and they indicate that the first half of the isolation period was the most difficult from the standpoint of adaptation. It is expressly at this time that the most drastic changes in affect were observed. This is also indicated by the data illustrated in Figure 3, which demonstrate the dynamic nature of changes in level of anxiety.

The high level of anxiety at the start of the wintering period is related to anticipation of the Antarctic winter, whereas the increased anxiety at the end of the expedition should be attributed to preparations for returning to

*Translator's note: No Figure 4 was included with this article.

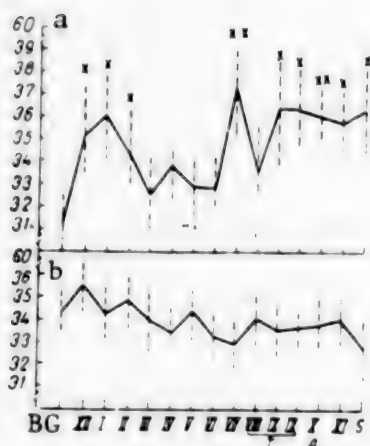


Figure 3.
Dynamics of anxiety level in expedition workers during year-long isolation

- a) anxiety as a state
- b) anxiety as a feature
- BG) background
- T) "quiet in the air" experiment
- A) "electric power plant accident" experiment
- S) study on shipboard, on trip home

former occupational and social roles (process of secondary adaptation). We were impressed by the elevated indicators of anxiety in July and September. They reflect the influence of deeper information deprivation and (in late September) the experimental accident at the power plant. The obtained data stress the fact that, during Antarctic isolation, there is an increased need for both specific and nonspecific information. A real threat (power plant accident) intensifies the stressogenic effect of social isolation.

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ADAPTIVE EFFECTS OF REPEATED IMMERSION ON MAN

Moscow KOSMICHESKAYA BIOLOGIYA I AVIAKOSMICHESKAYA MEDITSINA in Russian Vol 18, No 2, Mar-Apr 84 (manuscript received 31 Mar 83) pp 57-59

[Article by Ye. B. Shul'zhenko, V. G. Kozlova, Ye. A. Aleksandrova and K. A. Kudrin]

[English abstract from source] The effect of intermittent immersion on orthostatic tolerance, fluid-electrolyte metabolism and neuromuscular system was investigated. Control and experimental immersions were used. Experimental immersion was preceded by 12-hour exposure to immersion at night for three times. Experimental immersion was accompanied by reduced renal excretion of fluid, sodium and potassium and normalization of the muscle tone. After experimental immersion orthostatic tolerance approached the control level. The difference in the physiological effects of control and experimental immersions seem to be associated with the capacity of the human body to adapt to immersion, if it is applied intermittently.

[Text] It is known that there is a functional change in many systems of the body (including change in neuroreflex mechanisms of controlling arterial and venous tonus, decrease in muscle tone, development of signs of relative hypohydration, etc.) within the 1st-3d day of flight, which could lead to worsening of well-being and decrease in work capacity. Moreover, after returning to earth's gravity there is often development of orthostatic instability. The efforts of researchers are aimed at alleviating or compensating these signs.

In the system of measures to prevent the adverse effect of weightlessness on man, much attention is devoted to methods of preflight conditioning for redistribution of body fluids in a cranial direction [1, 2]. In particular, it has been suggested that head-down tilt (-5°) be used frequently during nocturnal sleep. Researchers noted that it is possible to then achieve under ground-based conditions a significant degree of adaptation to weightlessness. However, evaluation was made in the cited studies of only the general condition of subjects.

At the same time, it had been shown that immersion elicits deeper adaptive changes [3] than antiorthostatic [head-down] position (-6°).

For this reason, our objective here was to test the effect of repeated immersion on severity of physiological reactions inherent in the first day of exposure to simulated weightlessness, as well as on orthostatic stability.

Methods

The studies were conducted with the participation of 6 healthy men 25-35 years of age. The physiological effects of weightlessness were simulated by "dry" immersion (IM) lasting 36 h [4].

The tests were conducted on the following protocol: continuous IM for 36 h (IM-1)--3-day break--3 immersions at night for 12 h (intermittent IM; IM-2)--continuous IM for 36 h (IM-3).

We performed an orthostatic test (OT) lasting 20 min on a turntable with 70° tilt in the mornings after a light breakfast, before and after IM-1, as well as after IM-3. In the 1st, 5th, 10th, 15th and 20th min of the OT we took an EKG in the Neba leads, and recorded stroke (SV) and minute (MV) volumes of circulation using an RPG 2-02 tetrapolar rheograph. Blood pressure (BP) was measured with an AD-KTs instrument. Total peripheral resistance (TPR) was calculated using the Poiseuille formula.

During all of the periods of the study we kept track of 24-h fluid and electrolyte intake, concentration of sodium and potassium in urine by flame photometry, and calculated the difference between intake and output of these substances per day.

Tonometry of crural muscles (gastrocnemius--lateral and medial heads--GL and GM; anterior tibial muscle--ATM) and femoral muscles (quadriceps--lateral head--FQ) was performed under standard conditions at rest, before and after IM-1 and IM-3 with a tonomyometer [5].

All of the data were processed by the Student method of variation statistics.

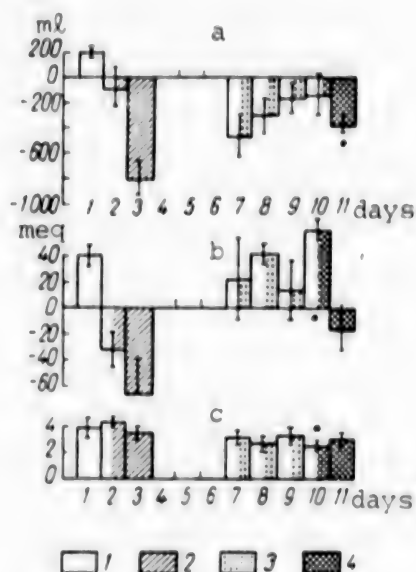
Analysis of the results enabled us to arbitrarily divide the 6 subjects into 2 groups according to tolerance of orthostatic tests after IM-1. The 1st group (4 men) consisted of individuals with good orthostatic stability and the 2d, of 2 subjects with low orthostatic stability.

Results and Discussion

The change from ordinary motor activity to water-immersion hypodynamia was associated with sensations of blood rushing to the head, congested nose, impairment of nocturnal sleep, diminished appetite and pain in the lumbar region in some of the subjects.

Such signs were not observed with IM-3.

The results of tests under IM-1 conditions are indicative of diminished muscle tone, by 8% in the gastrocnemius ($P < 0.02$) and 9% in the femoral muscles ($P < 0.02$). ATM did not change (see Table). No statistically reliable changes in muscle tone were demonstrated with IM-3.



Changes in parameters of fluid-electrolyte metabolism: differences between uptake and renal excretion of fluid (a), sodium (b) and sodium/potassium ratio in urine (c)

- 1) free motor activity
- 2) IM-1
- 3) IM-2
- 4) IM-3

*) $P < 0.05$ as compared to corresponding IM-1 period

even more marked sodium loss (see Figure). In the 2d group of subjects, sodium intake exceeded somewhat renal elimination throughout the IM-1 period.

With IM-2, there was less fluid loss through the kidneys, as determined by the difference between daily intake and output, whereas sodium excretion was less than intake. Only one of the subjects in the 2d group showed no decrease in sodium excretion.

The rate of renal excretion of fluid and sodium did not differ from background levels, either in the first 1.5 h of IM-3 or the subsequent night.

For the first 2 days (IM-3), the subjects in the 1st group showed less output of sodium than in the same period of IM-1, whereas in the 2d group more sodium was excreted.

We failed to demonstrate any distinct pattern of potassium excretion; however, analysis of dynamics of sodium/potassium coefficient in urine revealed changes in the same direction in all subjects. Thus, within somewhat less than a full 24 h of IM-1, the coefficient increased somewhat, as compared to the background level, whereas in the next 24 h it began to decline. IM-2 elicited

Measurement of muscle tone (in arbitrary units) after intermittent IM

| Test time | ATM | GL | GM | FQ |
|-------------|----------|----------|-----------|-----------|
| BACK-GROUND | 825 ± 15 | 755 ± 14 | 740 ± 17 | 785 ± 18 |
| M-1 | 812 ± 12 | 737 ± 9 | 680 ± 12* | 715 ± 15* |
| M-2 | 827 ± 16 | 728 ± 11 | 703 ± 16 | 732 ± 13 |

* $P < 0.02$ as compared to background.

The rate of renal excretion of fluid increased by 56% ($P < 0.05$) already within the first 1.5 h of IM-1. This was associated with a tendency toward increase in rate of sodium excretion. For the next 8 h (nocturnal sleep), the rate of renal excretion of fluid was the same, while sodium excretion rate was higher than in the same period of the background study ($P < 0.01$). For part of the first 24 h of IM-1, the difference between fluid intake and output was lower than in the background period, whereas in the next 24 h (2d day of IM-1) there was more fluid output than intake in all subjects (see Figure).

In the 1st group of subjects, sodium excretion exceeded intake already on the 1st day of IM-1. The 2d day was characterized by

even more marked sodium loss (see Figure). In the 2d group of subjects, sodium intake exceeded somewhat renal elimination throughout the IM-1 period.

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further decline of sodium/potassium ratio, and the 1st day of IM-3 was notable for the lowest value for this parameter ($P < 0.01$), as compared to the base level (see Figure, b).

After IM-1, we demonstrated a decrease in orthostatic stability of all subjects. In the 1st group of subjects, the heart rate (HR) increased by 89.9%, versus 76.1% before IM, while maximum HR constituted 118 ± 6 /min, versus 101 ± 9 /min before IM. The changes in SV before and after IM-1 were analogous and characterized by a 48-50% decline at the start and 64% at the end. MV during OT decreased by 34% by the 15th min. BP changes during the OT after IM-1 were insignificant and characterized by some elevation of diastolic pressure, with unchanged systolic pressure. TPR increased constantly and exceeded the base level by 81% ($P < 0.05$) by the end of the orthostatic test.

In the 2d group of subjects, the decrease in orthostatic stability was more marked after IM-1 than in the 1st group. In the 5th min, 1 subject developed a presyncopic state, 1 developed isolated extrasystoles in the 16th min, which had not been observed during the OT before IM.

After IM-2 followed by IM-3, endurance of orthostatic tests increased. Subjectively, well-being during the OT was better. Objective data confirmed this.

In the 1st group of subjects, maximum HR (99 ± 20 /min) and minimum SV (53 ± 9 ml) were close to the values before IM-1 (101 ± 9 /min and 47 ± 8 ml). Postural changes in HR and SV were similar to their values before IM-1. The decline of MV was even more marked, although the base level was lower. Pulse pressure remained unchanged, since systolic and diastolic pressure dropped to the same extent. TPR increased by 41%.

In the 2d group of subjects, after IM-3 the decline of MV during the OT was virtually the same as in the 1st group (1.8 l, or 26.6%), but occurred against a background of greater increment of HR (98%) and greater decline of SV (62%). BP underwent insignificant change, and we mainly observed some drop of systolic pressure. The TPR changes were of the same nature as in the 1st group of subjects.

The changes observed after IM-2 are apparently related to the body's capacity to adapt to various extreme factors when they recur frequently. However, the adaptive signs were more marked in the 1st group. The results of testing the 2d group are indicative of change in base state before IM-2, as compared to parameters for the 1st group. In particular, the relative hypohydration of the 2d group of subjects before IM-1 [6] could have affected the severity of changes in parameters of fluid-electrolyte metabolism. For this reason, the differences between the results under IM-1 and IM-3 conditions were not so substantial. At the same time, orthostatic stability of this group of subjects was lower after IM-1, whereas after IM-2 and IM-3 it was the same as in the 1st group.

With IM-3, the 2d group of subjects presented a tendency toward decreased excretion of sodium and preservation of muscle tone, which could be indicative of development of adaptive processes with repeated immersion. This assumption was also confirmed by the fact that the urine sodium/potassium ratio, which is an

indirect indicator of mineralocorticoid activity, changed in the same direction in both groups of subjects. Thus, intermittent IM lowered the severity of physiological reactions to subsequent 36-h IM and made it possible for man to retain resistance to postural tests.

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CIRCADIAN RHYTHM OF HUMAN HEART RATE DURING ANTIORTHOSTATIC TESTS

Moscow KOSMICHESKAYA BIOLOGIYA I AVIAKOSMICHESKAYA MEDITSINA in Russian Vol 18, No 2, Mar-Apr 84 (manuscript received 22 Nov 82) pp 60-63

[Article by L. Lhagwa (Mongolian People's Republic)]

[English abstract from source] The study of diurnal variations of heart rate of 7 healthy volunteers exposed to head-down tilting (-8°) demonstrated that the absolute value decreased at the peak phase and in the daytime and increased at night; the amplitude of the diurnal variations declined. The experimental data indicate that heart rate may decrease in the morning and in the daytime beginning with the first days of the head-down position. Sometimes this decrease may be delayed and develop on head-down days 7-12.

[Text] The heart rate (HR) is one of the informative indicators of the state of the cardiovascular system. The nature of changes in parameters of circadian rhythm of HR in man has been described by a number of authors in the aspect of space biorhythmology [1-5].

Our objective here was to study the circadian rhythm of HR in subjects submitted to head-down position for different periods of time.

Methods

In the course of this work, we conducted 2 series of observations with the participation of 7 healthy subjects. The first series lasted 18 days (including 7 days in antiorthostatic position, -8°) and the second, 32 days (12 days in head-down position).

HR was counted on the EKG, as well as by palpation on the right radial artery for 1 min after 5-min rest. During the waking period, from 0700 to 2300 hours, HR was measured at odd hours of the day in all series and at 0130 and 0500 hours during the sleep period. The obtained data were submitted to individual analysis, using the methodological procedures described by S. I. Stepanova [3] and Lhagwa [5]. The material was submitted to statistical processing by the usual methods with use of Student's criterion.

Results and Discussion

Analysis of data obtained in the course of recording the subjects' HR with head-down tilt revealed a decrease in values of this parameter at the maximum phase and in the daytime (Tables 1 and 2), increase in its values at night (Table 3) and decrease in amplitude of circadian HR rhythm. In the first series of studies, these signs were demonstrable for the first 7 days in antiorthostatic position (i.e., throughout the observation period) and in the second series, only in the second half of the study (from the 7th to 12th day, being more marked at the end of this period, i.e., 10th-12th days).

Table 1. Range of HR fluctuations (beats/min) in the course of 24-h periods at different stages of the study ($M \pm m$)

| Subject | Background | | Head-down | |
|---------|------------------|------------------|------------------|------------------|
| | maximum | minimum | maximum | minimum |
| 1 | 87.66 \pm 3.47 | 60.33 \pm 3.14 | 80.28 \pm 5.22 | 61.43 \pm 0.71 |
| 2 | 88.33 \pm 4.52 | 60.67 \pm 2.09 | 71.85 \pm 3.13 | 58.86 \pm 1.14 |
| 3 | 88.33 \pm 3.47 | 60.66 \pm 0.69 | 75.00 \pm 5.22 | 55.29 \pm 0.43 |
| 4 | 70.35 \pm 0.31 | 53.92 \pm 1.77 | 69.42 \pm 0.18 | 56.92 \pm 1.60 |
| 5 | 78.36 \pm 0.38 | 57.50 \pm 1.42 | 77.42 \pm 0.83 | 57.75 \pm 0.71 |
| 6 | 76.58 \pm 0.34 | 56.58 \pm 1.60 | 74.75 \pm 0.44 | 62.00 \pm 0.71 |
| 7 | 74.50 \pm 0.37 | 56.08 \pm 1.24 | 72.42 \pm 0.35 | 57.67 \pm 0.80 |

Table 2. Mean daily HR (beats/min) in antiorthostatic position ($M \pm m$)

| Subject | Back-ground | Head-down tilt | <i>p</i> |
|---------|------------------|------------------|----------|
| 1 | 77.50 \pm 1.33 | 72.36 \pm 0.88 | <0.001 |
| 2 | 71.10 \pm 1.99 | 66.26 \pm 0.60 | <0.01 |
| 3 | 72.16 \pm 2.06 | 64.83 \pm 0.99 | <0.01 |
| 4 | 68.39 \pm 0.48 | 66.33 \pm 0.23 | <0.01 |
| 5 | 74.78 \pm 0.62 | 69.90 \pm 0.56 | <0.01 |
| 6 | 72.18 \pm 0.42 | 70.73 \pm 0.37 | <0.01 |
| 7 | 69.32 \pm 0.57 | 66.48 \pm 0.48 | <0.01 |

D. G. Maksimov and M. V. Domracheva [6] reported lowering of HR in the 1st week of head-down tilt (-4°). In the studies of A. V. Beregovkin and V. V. Kalinichenko [7], the subjects' HR remained below background values up to the 14th day, right after waking in antiorthostatic position. Some slowing of HR in head-down position was reported by K. L. Geykhman and M. R. Mogendovich [8]. In the study of A. D. Voskresenskiy et al. [9], a delayed pulse reaction was demonstrated to continuous and prolonged head-down tilt: the subjects' HR dropped slightly by the 3d-4th day in antiorthostatic position (-4°).

Thus, both our data and some of those in the literature indicate that HR may decrease in the morning and daytime already on the 1st day in antiorthostatic position, but this decline could be deferred and appear only in the 3d-4th day or even later (7th-12th day).

The decline of HR per se, other conditions being equal, leads to decrease in minute blood volume. The facts indicate, however, that with the change to head-down position, minute volume does not decrease in man, rather it increases due to increase in venous return. No doubt, when delivery of blood to the head increases a decline of minute volume would be desirable, and it must be stated

that it is expressly in the head-down test that one observes such a tendency (bradycardia) as a reflex to drastic elevation of pressure in the carotid arteries [10]. However, in the presence of increased venous return it is apparently necessary, first of all, to compensate for this phenomenon by augmenting the carrying capacity of the heart by means of increasing stroke and minute volumes. Probably this is why a decline of pulse rate from the very start of the antiorthostatic test is not observed always by far. It is believed that such a decline develops if there is rapid decrease in circulating blood volume. From this point of view, the decline of HR in head-down position should be interpreted as the result of successful development of adaptive hemodynamic changes. This is exactly how D. A. Alekseyev et al. [10] assess the HR drop in head-down position. HR probably declines in antiorthostatic position in those people in whom the process of deposition of blood and intensive elimination of fluid starts from the very first minutes in this position. If, however, the process of reduction in circulating blood volume develops slowly, HR does not decrease at the first stage of head-down position. If this is indeed so, the reaction of HR decline in head-down position (its severity and speed of occurrence) could serve as a gage of activity of the adaptation process.

Table 3. HR dynamics at night in some subjects on 10th-12th day of head-down position

| Ulan-Bator time, hours | Subjects | | | |
|---------------------------|---------------|---------------|---------------|---------------|
| | 4 | 5 | 6 | 7 |
| 1.00 | 64.33 (57.00) | 65.33 (60.91) | 70.00 (62.08) | 63.66 (59.83) |
| 3.00 | 66.00 (61.00) | 64.00 (61.33) | 64.33 (61.16) | 62.66 (61.33) |
| 5.00 | 62.67 (57.75) | 64.33 (60.08) | 63.33 (59.75) | 59.25 (59.50) |
| 7.00 | 68.00 (64.41) | 59.00 (68.41) | 68.66 (66.08) | 66.33 (65.66) |

Note: Background HR is given in parentheses.

It must be stressed that when we refer to decrease of HR in head-down position, we have in mind the results of recording this functional parameter only in the daytime. The absolute majority of researchers do not report the time of day at which they observed the HR decrease in antiorthostatic position. We, however, observed such a decline only in the daytime. The nocturnal period was characterized by increase in HR values, and we distinctly observed it in the interval from the 10th to 12th day of head-down position. It is rather difficult to explain such an increase. We cannot rule out the possibility that its cause is referable to the methodological distinctions of recording the HR. The fact of the matter is that, at night (as in the daytime), this parameter was often determined in the subjects by palpation. If we assume that sleep is poorer in head-down position, particularly on the 10th-12th days, apparently the physician's contact with the subject's arm could be associated with the latter's abrupt arousal and consequent increase of HR. A. D. Voskresenskiy et al. [9] and V. M. Mikhaylov et al. [11] have reported worsening of sleep during long-term head-down tilt. The data of V. N. Artishuk et al. [12] are of particular interest; they report that, for the first 3-4 days in head-down position, their subjects retained good mental tonus and reported no sleep disorders

whatsoever, whereas in the period from the 5th to 15th days they presented a decline of mental tonus, unstable affect, outbursts of irritability and worsening of sleep.

In our studies, we did not determine the quality of sleep of our subjects, but on the basis of the data submitted by V. N. Artishuk et al. [12], there are grounds to attribute the increased HR at night to poorer sleep in the period from the 10th to 12th days of head-down position.

It is interesting to examine another possible mechanism of HR increase at night. From about the 4th-5th week of antiorthostatic hypokinesia, some authors [6, 13] observed an increase in pulse rate (unfortunately, they do not indicate the time of day when this happened), which they attributed to development of hypodynamia due to prolonged immobility. Perhaps, in our studies too, the increased HR in the 2d week of antiorthostatic hypokinesia was also an early manifestation of hypodynamia. It may be that, at night, the HR is the most sensitive to the hypodynamia factor, and for this reason change therein is demonstrable at an earlier time than the same reaction in the daytime. This question has yet to be answered.

We must also mention the more distinct localization of HR minimum on the 24-h scale with increase in duration of head-down position, as observed in our studies. This phenomenon indicates that stress could cause the rhythm to be more distinct, more accentuated. A very distinct rhythm (and in particular, a circadian one) is not necessarily evidence of well-being. There are grounds to discuss optimum distinction of a vital (biological) rhythm. Any deviation, both in the direction of lesser or greater distinction, is indicative of development of stress.

As for the decrease in amplitude of circadian rhythm of HR, which we observed under antiorthostatic conditions, it is no doubt attributable to decrease in HR at the phase of its diurnal maximum and also, in part (i.e., in those cases where it was observed), to increase in HR values at the phase of the diurnal minimum. Thus, analysis of our findings warrants the statement that head-down position alters the parameters of man's circadian HR rhythm.

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EFFECT OF WORKING IN TWO SHIFTS ON CIRCADIAN RHYTHM OF HEART RATE

Moscow KOSMICHESKAYA BIOLOGIYA I AVIAKOSMICHESKAYA MEDITSINA in Russian Vol 18, No 2, Mar-Apr 84 (manuscript received 9 Jun 83) pp 63-66

[Article by A. I. Shchukin]

[English abstract from source] Circadian variations of the heart rate of 58 male workers, aged 18-21, were investigated. The builders were from different geographical areas and their work record at the construction site was 2 months, 1 or 2 years. Some of the test subjects worked only in the daytime (8 a.m. to 5 p.m.) and others worked in two shifts (day and night, 5 p.m. to 1 a.m.), with the two shifts alternating weekly. Physical examinations were performed next day after the working week (those who worked in two shifts were as a rule examined after night shift). Heart rate was determined from ECGs (recorded in the II standard lead at 2-hour intervals during 24 hours; at night electrode fixation naturally disturbed the test subjects). The builders whose work record was 2 months showed an inverted heart rate: normal increase in the daytime and decrease at night was reversed and night values were greater than daytime values. This can be considered as a manifestation of anxiety due to an early change in the social, geographical and everyday environment. The builders whose work record was 1 or 2 years did not show such changes. The workers who worked in two shifts showed larger amplitudes in the circadian rhythm of heart rate, irrespective of their work record. This can be regarded as a manifestation of stress due to the night shift or continuous changes from one shift to the other.

[Text] The influence of working in shifts on man is presently being studied as it relates to various occupations, including aviation, where there are many flights in the early morning, evening and night hours. Use of shift schedules in cosmonautics is not ruled out either, for example, when it is necessary to take on watch duty in a spacecraft continuously, around the clock.

Our objective here was to make a comparative study of circadian rhythm of heart rate (HR) as related to working for different periods of time (2 months, 1 and 2 years) on one and two shifts.

Methods

A total of 58 men 18-21 years of age, who came from different climate and geographic regions of our country, participated in this study. Some subjects work on one shift (morning), some on two shifts--morning and evening--alternating the shift each week. The work hours for the morning shift were from 0800 to 1700, and for the evening shift, 1700 to 0100 hours. Sleep period was from 2130 to 0530 hours when working on the morning shift and from 0130 to 0930 hours on the evening shift.

The subjects were divided into six groups (group characteristics are listed in Table 1), depending on work tenure and shifts (one or two-shift work).

The workers were examined at a clinical hospital on the day after finishing the work week. All individuals working on the two-shift schedule were examined after the evening shift, the fourth group was additionally examined after the day shift also (see Table 1).

Table 1. Characteristics of groups of subjects

| Group | Number of subjects | Tenure | Number of shifts |
|-------|--------------------|----------|------------------|
| 1 | 18 | 2 months | 1 |
| 2 | 5 | | 2 (PM) |
| 3 | 10 | | 1 |
| 4 | 5 | 1 year | 2 (AM and PM) |
| 5 | 10 | | 1 |
| 6 | 10 | 2 years | 2 (PM) |

Key: PM) examined after evening shift
AM) examined after day shift

Upon finishing the day shift, the subjects arrived at the hospital at 2000 hours, and after the evening shift, at 0200 hours. We started recording HR in the morning (at 0700 hours) and then regularly every 2 h up to 0700 hours the following morning. HR was determined from the electrocardiogram (EKG) recorded in the second standard lead using an Elcar-6 oscillography. The EKG's were taken with subjects in supine position. In the period from 0900 to 2300 hours, the subjects remained in this position for 30 min prior to taking the EKG; at 0100, 0300, 0500 and 0700 hours, the subjects sleep was disturbed to take the EKG (in particular, to place the electrodes).

The tracings were made at paper feed rate of 50 mm/s for 10-15 s (1st and 2d groups) and 40-45 s (3d-6th groups).

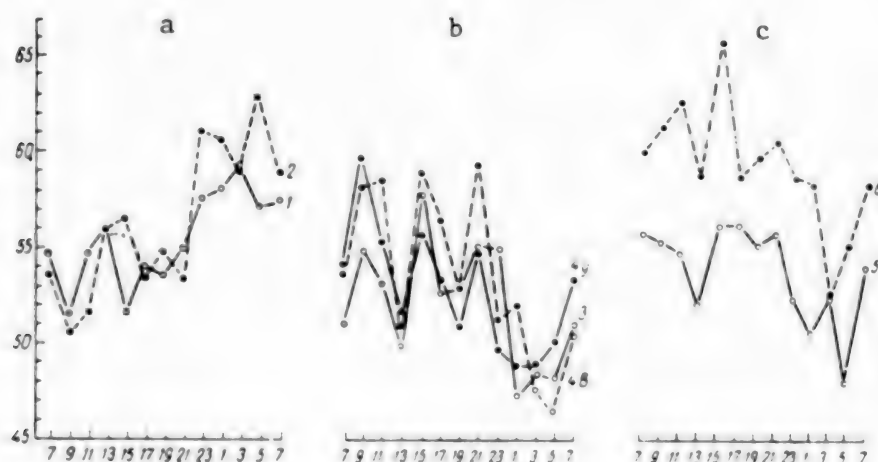
Using a millimeter ruler, we measured duration of R-R intervals on the EKG's of subjects in the 1st and 2d groups (within each interval we used the whole number of millimeters in it; fractions of a millimeter were disregarded), then we calculated the arithmetic mean for each tracing, which was then converted to the HR parameter (per min) from a table. On the EKG's of subjects in the

3d-6th groups, we counted the number of R waves per 30-s interval, and multiplied the result by 2.

The subjects engaged in the usual activities in a hospital during the tests (reading, watching television, playing table games). Only individuals who were essentially healthy participated in the study, and they had undergone a preliminary general physical.

Results and Discussion

The Figure illustrates the mean group 24-h HR curves for the subjects. In representatives of the 1st and 2d groups (a), we were impressed by the unusual relationship between day and night parameters: as a rule, HR is slower at night, but in this case the night parameters were appreciably higher than the daytime ones. In both groups of subjects this difference was statistically significant (Table 2). Evidently, the unusual new social and everyday situation for individuals in these groups and related anxiety (it should be recalled that the subjects were inevitably aroused at night, when electrodes were placed) were the chief causes of such profound changes in circadian HR rhythm.



Circadian variations of subjects' HR (mean group data). X-axis, Moscow time (hours); y-axis, HR (per min)

a, b, c) tenure: 2 months, 1 and 2 years

1-6) groups

y, b) on curve for 4th group--tested after daytime and evening shifts

A comparison of the curves for the 1st and 2d groups shows that the amplitude of circadian HR rhythm (difference between maximum and minimum HR) was wider in the 2d group than the 1st, and this was chiefly due to increase in maximum HR. A statistical comparison of individual daily amplitude of HR in the 1st and 2d groups showed substantial differences (Table 3). On the basis of data in the literature which are indicative of increased amplitude of biological

fluctuations under stress [1-5], it can be assumed that the higher amplitude in this case is indicative of stress due to working two different shifts by representatives of the 2d group, or to the fact that these subjects worked the evening shift the previous week (after which they were examined).

Table 2. HR (per min) in day and night hours in subjects of 1st and 2d groups (according to mean group curves illustrated in Figure)

| Parameter | Group | |
|---|------------|------------|
| | 1 | 2 |
| Mean day value (0700 to 2100 hours) | 53.9 | 53.8 |
| Mean night value (2300 to 0700 hours the next morning) | 57.8 | 60.4 |
| Difference between mean night and mean day values | 3.9 | 6.6 |
| Statistical rating of significance of differences by series criterion | $P < 0.05$ | $P < 0.05$ |

The curves for individuals in the 3d and 4th groups are compared in the Figure, b. The parameters for the 3d group of subjects are shown by one curve and for the 4th, by two, one of which was plotted after working 1 week on the day shift and the other, after a week's work on the evening shift. All of the curves have the usual appearance, with higher values for HR in the daytime and decline of this parameter at night. In other words, after working for 1 year, disturbances referable to circadian HR rhythm that were noted in subjects with 2-month tenure were no longer demonstrable. This can be interpreted as a manifestation of adaptation to new living conditions.

The marked similarity of configuration of all three curves does not permit detection of an overt indication of work on the same or two shifts. It should be noted that the range of minimal values on curve 4b (0300-0500 hours) is shifted toward the right boundary of the range of minimal values for curves 3 (0100-0500 hours) and 4y (2300-0500 hours). This suggests that the difference in curve 4b is attributable to the influence of the evening shift: in the case of late end to the work shift and, accordingly, late bed time, minimal HR during sleep is also reached at a later time than when working the day shift. It is important to note that this "trace" of the evening shift (delayed minimum) persists for at least the next 24 h after the work week, and it is demonstrable under conditions of physical and emotional quiet (just like, incidentally, the "trace" of the day shift--relatively early appearance of HR minimum). In other words, some of the distinctions of circadian variations of HR due to working on the evening (or day) shift have time to become fixed by the end of the week, and for this reason the weekly change from one shift to the other is associated with weekly change in these distinctions (elimination of former features, formation and fixation of new ones), which no doubt is a strain on adaptation mechanisms. The weekly alternation of shifts is in essence nothing other than rhythmic, pulsed stimulation, where each pulse (change from shift to shift) elicits an adaptive response, i.e., generates stress.

Table 3.
Amplitude of circadian rhythm of
HR (per min) in subjects (M±m)

| Group | Amplitude |
|-------|--------------|
| 1 | 12,6±0,69 |
| 2 | 15,0±1,94* |
| 3 | 12,6±1,41 |
| 4 | 14,0±3,16** |
| 5 | 15,6±2,58** |
| 6 | 12,2±1,89 |
| 6 | 17,0±1,73*** |

- *) Difference is statistically reliable, as compared to 1st group ($P < 0.05$)
- **) Difference is statistically unreliable, as compared to 3d group ($P > 0.05$)
- ***) Difference is statistically reliable, as compared to 5th group ($P < 0.05$)

there were 2-3 people with individually high HR among the 6th group of subjects, and they caused the 24-h group mean curve to be higher. However, a close scrutiny of individual HR values for the 5th and 6th groups failed to demonstrate a difference between them in this respect and, consequently, our initial assumption was not confirmed. It should be noted that a number of authors relate the increase in pulse rate to fatigue and overfatigue. G. Leman, referring to the studies of Bartenwerthen, mentions the higher HR in the presence of fatigue [6]. In athletes, overfatigue is associated with quickening pulse [7]. The possibility cannot be ruled out that, in this case too, the high HR in the 6th group is a sign of fatigue (or start of overfatigue), which did not reach a marked degree and was attributable to prolonged (2 years) work on two different shifts.

According to A. D. Slonim (quoted in [8]), as applied to a functional parameter that is characterized by a reduction of numerical values from daytime to night hours, the most reliable sign of fatigue is slower decline of recorded values at night. As can be seen in the Figure, c, such slower decline was inherent in the 6th group of subjects, unlike parameters for the 5th group, which could be viewed as either a "trace" of the evening shift or evidence of fatigue due to prolonged work on two different shifts.

Higher daytime values for HR and decline of this parameter at night, with minimums at 0500 hours (work on the same shift) and 0300 hours (work on two shifts), were typical of the curves of HR changes in the 5th and 6th groups. In other words, the usual daytime and night pattern of HR levels is inherent in these groups of subjects.

We can add to the foregoing that, as can be seen from Table 3, when one works continuously on the same shift for 1 year (3d group), the amplitude of circadian HR rhythm was lower than when working on two different shifts for the same period of time (4th group). And, although this difference is statistically insignificant, it is relevant in the light of the above-mentioned link between amplitude of biological rhythm and stress due to working in shifts; the possibility cannot be ruled out that, in this case, the higher amplitude in representatives of the 4th group who worked alternately on two different shifts is indicative of greater stress than in the 3d group.

The 24-h HR curves for subjects in the 5th and 6th groups are illustrated in the Figure, c. Here, we are impressed, first of all, by the difference in levels of the two curves. In an effort to explain this difference, we first assumed that

In view of the difference in level, it is difficult to compare (visually) curves 5 and 6 with regard to amplitude but, as can be seen in Table 3, the individual amplitudes of circadian variations of HR were greater on the average in the 6th group of subjects than in the 5th, which could be attributed to the stress effect of working on two shifts, or else to working on the night shift prior to examining the 6th group of subjects.

Thus, it was established that by the end of a 2-month period of tenure, i.e., after changing the customary social, living and, in a number of instances, climate conditions, the circadian HR rhythm in the case of both single and two-shift work was drastically impaired: instead of the usual increase of HR in the daytime and decrease at night, we observed the reverse. Upon reaching 1 and 2 years' tenure, such disturbances were not demonstrable.

Unlike working on the same shift, whatever the tenure (2 months, 1 and 2 years), there was greater amplitude of HR circadian variations when working on two different shifts. Since the individuals working on different shifts were examined more often after working 1 week on the evening shift, it is difficult to state with certainty what caused the increase in amplitude: work in the evenings or the fact that it was done on different shifts, i.e., with constant change from one shift to another. In any case, the higher amplitude of circadian rhythm of HR can be evaluated as a manifestation of stress.

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EFFICACY OF CONDITIONING ANIMALS TO HYPOXIA DURING SLEEP

Moscow KOSMICHESKAYA BIOLOGIYA I AVIAKOSMICHESKAYA MEDITSINA in Russian Vol 18, No 2, Mar-Apr 84 (manuscript received 3 Jan 83) pp 67-70

[Article by V. B. Malkin and N. F. Landukhova]

[English abstract from source] In sleeping animals (sleep induced by the drugs aminasine and elenium) step-by-step training for 13 days (6 hours daily) in an altitude chamber produces a number of adaptive changes--hemopoiesis stimulation, slower weight gain, increased adrenal weight and, this being most important, elevated altitude tolerance. It is concluded that the state of drug-induced sleep can be well used to train for altitude hypoxia.

[Text] The question of possibility of developing adaptation to hypoxia through conditioning only during sleep had not been explored heretofore. Moreover, there are no sufficiently reliable data in general about whether it is possible to fix (retain) any trace of various stimuli if they are regularly used only during sleep. For this reason, we undertook an experimental investigation of the possibility of developing adaptation to altitude hypoxia in animals that were asleep in a pressure chamber during the conditioning period.

Such a study could be not only of theoretical interest, but of practical significance. If the possibility of developing adaptation to hypoxia by conditioning during sleep is experimentally proven, it will be possible to use such conditioning in altitude physiology, space and sports medicine.

Methods

The difficulty of the experimental approach to the study of animal conditioning to hypoxia during sleep is related to the species-specific distinctions of spontaneous sleep in different animals. The species-specific distinction of sleep in laboratory animals that are the most often used to study hypoxia (white mice and rats) is polysomnia. According to the data of Clancy et al. [1], who made extensive use of polygraph tracings of sleep and cinematography of animal behavior, in the course of a day (from 0800 to 2000 hours) rats wake up 396 times, i.e., there is a high frequency of alternation of sleep and waking state. Thus, natural sleep in these animals does not permit the study of the effect of hypoxia and conditioning to it selectively, only during sleep. For

this reason, it is possible to condition white rats to hypoxia during sleep only if pharmacological agents are used that induce a stationary sleep state. For this purpose, we chose the neuroleptic, aminazin, and the tranquilizer, chlordiazepoxide (elenium).

Experiments were conducted on 72 white mongrel male rats weighing 200-240 g. The animals were divided into 6 groups. Three groups of animals were submitted to altitude conditioning in a pressure chamber. Two groups were given pharmacological agents daily to alter the functional state of the central nervous system (20-25 min before "ascent") while in the pressure chamber: one group was given aminazin intramuscularly at the rate of 10 mg/kg weight and the other, elenium, intragastrically through a tube, in a dosage of 50 mg/kg weight. The third group consisted of intact control animals.

For a control, we used three more groups of animals that were kept in the vivarium all of the time on an identical diet. Two of these groups were given the same doses of agents as animals conditioned in the pressure chamber, while the third group consisted of intact animals.

The experimental results revealed that, when animals are given aminazin in a dosage of 10 mg/kg and elenium in a dosage of 50 mg/kg, they became immobile, reacted sluggishly to exogenous stimuli, becoming drowsy and falling asleep within 15-20 min, sleep lasting 7-8 h. Thus, we achieved our main goal: the animals were conditioned to low barometric pressure while asleep, as indicated also by the results of electroencephalography.

It should be noted that the animals developed a drowsy state and fell asleep faster after being given aminazin than elenium. Those given aminazin tolerated conditioning in the pressure chamber worse (particularly at "altitudes" of more than 6000 m). After termination of the conditioning ascents to "altitudes" of 6500-7000 m, their fur became ruffled and moist; 2 rats of this group expired on the 8th day of conditioning at an "altitude" of 6500 m, for which reason conditioning time for this group of animals was reduced to 3 h for the next 5 days (at "altitudes" of 6500-7000 m).

The animals were submitted to conditioning to low barometric pressure daily, with the exception of Sundays, for 6 h in the pressure chamber following a previously tested protocol: 1st day 3000 m, 2d day 4000 m, 3d day 4500 m, 4th day 5000 m, 5th and 6th days 5500 m, 7th day 6000 m, 8th and 9th days 6500 m, 10th day 7000 m, 11th day 6500 m, 12th and 13th days 7000 m.

To assess the effectiveness of adaptation to hypoxia, we determined altitude tolerance on the 2d day after completion of the entire conditioning cycle: animal survival time at high altitudes. For this purpose, they were submitted to stepped "ascent" in the pressure chamber at the rate of 80-100 m/s, first to an "altitude" of 10,000 m with a 10-min plateau, then ascent was increased by 1000 m with a 5-min plateau at each successive altitude. We placed one animal from each tested group in the pressure chamber at the same time, so that control and conditioned animals were subject to the identical conditions at high "altitudes." Individual animal resistance (altitude ceiling) of each animal was determined from the time that respiration stopped.

In addition to determination of altitude resistance, in the course of the experiment we made hematological tests on the animals: erythrocyte count and hemoglobin of peripheral blood, weight of body and adrenals. A comparison of physiological changes and levels of altitude resistance in intact animals kept in the vivarium and submitted to conditioning enabled us to assess the efficacy of pressure-chamber conditioning, as well as conditioning achieved in other groups. Blood was drawn from the tip of the animals' tail. We counted red blood cells per mm³ peripheral blood and determined hemoglobin concentration. Erythrocytes were counted by the photocolormetric method using an FEK M-60 [colorimeter] in a beam passed through a red filter, using a previously described technique [2, 3]. Hemoglobin concentration was determined photometrically with an FEK M-60 in a beam passed through a green filter, by the method in [4].

Immediately after death of experimental animals, the adrenals were extracted, fatty tissue removed from them, and both were weighed together on a torsion balance with 0.1 mg margin of error. To determine the rats' weight, they were weighed on a scale with pan before and after conditioning.

We used the parametric criterion of Student in statistical processing of the data. Calculation of parameters of normal distribution was made using an M-222 computer.

Results and Discussion

Administration of the pharmacological agents affected the pattern of change in body weight (Figure 1). The rats are one of the animal species that grow throughout their life. Altitude conditioning, as already indicated by many researchers [5, 6], slows down animal growth and weight gain. This was also confirmed in our experiments. Administration of aminazin slowed down weight gain. The weight gain was also slowed down by the conditioning to hypoxia and particularly as a result of giving this agent.

Elenium had an insignificant effect on weight gain in the control, but was instrumental in gain during pressure chamber conditioning. Thus, we demonstrated reliable differences in dynamics of body weight between animals given aminazin and elenium.

Figure 2 illustrates data on survival time of animals in different groups at high altitude. Analysis of these data shows that resistance to acute hypoxia increased reliably ($P < 0.01$) in the course of conditioning in all groups of rats.

Figure 2 shows that animals conditioned after being given aminazin and intact conditioned animals presented about the same degree of increase in altitude tolerance; after being given elenium, conditioning led to somewhat less but also quite reliable increase in resistance to altitude. Administration of aminazin and elenium to control animals lowered resistance to altitude somewhat ($P > 0.05$).

Analysis of the scatter of individual levels of resistance to altitude in each of the above-mentioned groups was indicative of their heterogeneity. Each group of unconditioned animals can be arbitrarily divided into three subgroups: those with low, average and high resistance to acute hypoxia. The animals with

low resistance consisted of rats with no more than 5 min survival time at an "altitude" of 10,000 m. The subgroup with average resistance consisted of animals who survived at this "altitude" for no more than 10 min. Highly resistant animals were those that survived at the "altitude" for over 10 min.

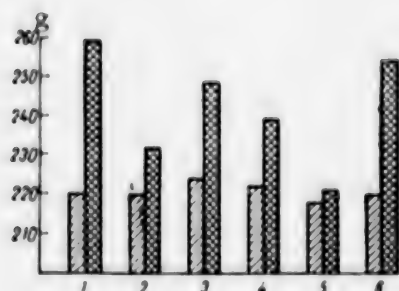


Figure 1.

Dynamics of change in body weight as a result of altitude conditioning and giving pharmacological agents.

Control groups: intact animals (1), with aminazin (2), with elenium (3). Experimental animals: intact (4), with aminazin (5), elenium (6). Crosshatched bars, before experiment; black bars, after experiment

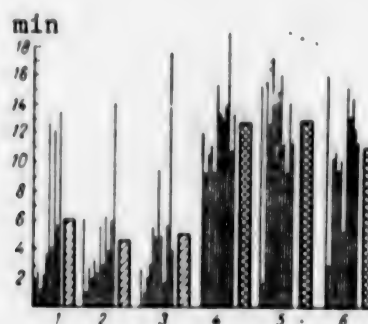


Figure 2.

Ceiling for different animal groups

Control groups: intact animals (1), with aminazin (2), with elenium (3). Experimental groups: intact (4), with aminazin (5), with elenium (6). Y-axis, survival time for different groups at high altitudes. Vertical lines, individual resistance; crosshatched bars, mean group resistance

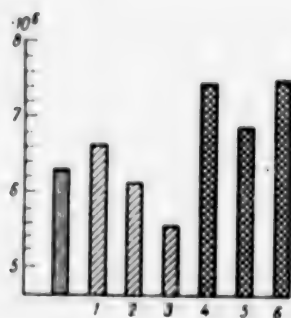


Figure 3.

Change in red blood cell count as a result of giving aminazin and elenium, as well as due to altitude conditioning. Bars with vertical stripes, background; with diagonal stripes, control; black bars, conditioning 1-6) same as in Figure 1.

During conditioning to hypoxia group heterogeneity diminished, and there was considerable decrease in differences between individual levels of altitude resistance. Examination of the bars illustrated in Figure 2 shows that the first group (clean control) consisted of 6 animals with low resistance to high altitude, 1 with average and 3 with high resistance. After conditioning in the pressure chamber, altitude resistance improved: average stay at a high "altitude" increased from 6 to 12.8 min, and there were no longer any animals with low resistance: minimum survival at a high "altitude" constituted 9.5 min in 2

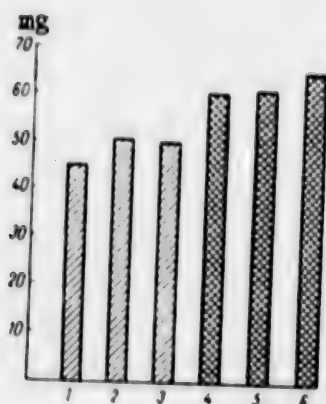


Figure 4.

Dynamics of change in adrenal weight in different animal groups as a result of altitude conditioning. Crosshatched bars--control; black--conditioning

1-6) same as in Figure 1

animals and exceeded 10 min in the rest (4th group).

Similar changes in individual resistance as a result of conditioning were noted in the rat groups given aminazin and elenium. Thus, in the 2d group of animals, which were given aminazin and stayed in the vivarium throughout the study, 7 rats presented low resistance, 4 average and 1 high. After conditioning (5th group), only 1 rat had low resistance and 1 average, while the remaining 10 had high resistance. In the 3d group, which was given elenium and remained in the vivarium all the time, 8 rats had low resistance, 3 average and 1 high. As a result of pressure-chamber conditioning, the individual resistance to hypoxia changed in such a manner (6th group) that 1 animal remained with low resistance, 2 with average and the other 9 with high resistance. Average survival at high "altitude" increased from 5 to 11 min.

Thus, the increase in resistance as a result of conditioning was attributable mainly to its considerable growth in rats with initially low resistance.

The hematological studies revealed that administration of pharmacological agents--aminazin and elenium--per se elicits some depression of hemopoiesis. This reaction was particularly marked after daily administration of elenium for 2 weeks (Figure 3). Conditioning to hypoxia elicited stimulation of hemopoiesis in both control animals and those given these agents. The increase in hemoglobin corresponded to increase in erythrocyte count.

During conditioning, the depressing effect of elenium on hemopoiesis gradually declined, as a result of which red blood cell count and hemoglobin were the same in conditioned animals (both intact and those given elenium). The depressing effect of aminazin on hemopoiesis persisted, so that red blood cell count and hemoglobin were reliably lower in conditioned animals given aminazin than in conditioned animals of other groups.

It is interesting to obtain information about adrenal morphology in order to evaluate the mechanism of adaptation to hypoxia. For this purpose, we weighed the adrenals of all experimental animals. Analysis of the findings revealed (Figure 4) that aminazin and elenium per se cause some increase in adrenal mass. Conditioning to hypoxia was associated with reliable elevation of this parameter (by 21-35%).

According to many authors [7-9], an increase in resistance to various adverse environmental factors with triggering of nonspecific adaptation mechanisms is observed in experimental animals concurrently with adrenal hyperfunction and

increased in their mass. This reaction also occurred in the experiments that we conducted.

The experiment results indicate that, for animals in a state of drowsiness and asleep due to administration of aminazin and elenium, conditioning to hypoxia in a pressure chamber, as well as in intact waking animals, elicits a set of adaptive changes: stimulation of hemopoiesis (increased red blood cell count and hemoglobin in peripheral blood), slower weight gain, increase in weight of adrenals and, what is the most important, increase in resistance to altitudes. This warrants the conclusion that a change in functional state of the central nervous system (drowsiness and sleep) does not prevent development, in the course of repeated exposure to hypoxia, of either specific (stimulation of hemopoiesis) or nonspecific (adrenal hyperfunction and increase in mass, slower weight gain) adaptive reactions, as a result of which the body's adaptation reserves increase.

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MORPHOLOGICAL STUDY OF PRIMATE MUSCLE FIBERS AND MICROCIRCULATION DURING
HEAD-DOWN HYPOKINESIA

Moscow KOSMICHESKAYA BIOLOGIYA I AVIAKOSMICHESKAYA MEDITSINA in Russian Vol 18,
No 2, Mar-Apr 84 (manuscript received 17 Jan 83) pp 71-73

[Article by Ye. I. Il'ina-Kakuyeva]

[English abstract from source] Primates were exposed to head-down tilt for 7 and 12 days. As the study continued, the body mass and muscle mass decreased, muscles became atrophic, and the number of functioning capillaries lessened. Out of the three muscles examined (gastrocnemius, soleus, and biceps brachii), the soleus muscle showed the greatest changes. It can be concluded that, in spite of blood redistribution and blood pooling in the upper body (seen during autopsy), no blood displacement occurs in the microcirculatory bed. The decrease in the number of functioning capillaries is normally regarded as a change that is concomitant with muscle atrophy.

[Text] It is known that weightlessness elicits redistribution of blood and fluid in the body, they shift from the lower part of the body to the upper. Measurement of the body's center of mass, which was done aboard Skylab-3, showed that the shift in body fluids in a cranial direction persists throughout the flight. This is associated with significant reduction of leg volume and decrease in tonus of crural veins. At the same time, there is insignificant change in arm volume [1, 2]. A similar shifting of blood, but less marked, occurs in hypokinetic subjects, particularly with antiorthostatic [head-down] hypokinesia (AOH) [3, 4], so that this condition could be used as a model to investigate some of the hemodynamic distinctions observed in weightlessness [5]. In particular, studies of peripheral circulation revealed that, with increase in flow of blood to the head there is decrease in volume and velocity of blood flow in vessels of the toes, increase in tonus of arterial vessels [6], decrease in number of functional capillaries in the digital nail bed [7]. These facts, which were established by physiologists, are indicative of circulatory change in the legs when blood is redistributed in the body, but they do not answer the question of whether the microcirculatory bed of muscles is affected, where a marked atrophic process [8] is observed under hypokinetic conditions (and in weightlessness) and there could be functional impairment of the muscle pump. Moreover, still open is the question

of whether there are differences in condition of the microcirculatory bed of muscles of upper and lower extremities, i.e., in muscles that differ in function and with different blood supply. We tried to answer this question in our morphological investigation.

Methods

The material was obtained from a combined morphological and physiological experiment conducted at the Institute of Experimental Pathology and Therapy, USSR Academy of Medical Sciences. We used 3 monkeys (*Macaca rhesus*, males), which had been kept for 7 days on special cots in clinostatic position then for 12 days with the head down at an angle of -6° . In the other group, 2 monkeys were kept in clinostatic position for 2 days and antiorthostatic position at the same angle for 7 days. Three monkeys served as a control, and they were kept in large cages where they could move about freely. The animals were sacrificed by intravenous injection of 2-3 ml 10% hexenal solution, and death was instantaneous. For our study, we took two muscles from the lower extremities (gastrocnemius and soleus) and one from the upper extremities (brachial biceps). The muscles were weighed, specimens were fixed in 10% formalin prepared on phosphate buffer, pH 7.2, and imbedded in histoplast. Functional capillaries in cross sections of muscles were demonstrated by staining the red blood cells in them with iron hematoxylin according to Heidenhain. We counted the functional capillaries per 500 muscle fibers. On parallel sections stained with picronigrosin, we made gravimetric determination of cross-section area (CSA) of muscle fibers, for which purpose the preparations were photographed, negatives projected on paper, on which we outlined 100 each of red, white and intermediate fibers. The outlined fiber projections were cut out and weighed on an electronic balance, with determination of mean mass per muscle fiber, which expressed the CSA of the fiber in arbitrary units. For a general histological examination, sections of muscles were stained with hematoxylin, eosin and by the Mallory method.

Results and Discussion

First of all, it must be noted that necropsy of experimental animals revealed distinct signs of redistribution of blood in the form of severe plethora of organs and tissues of the upper half of the body.

The Table shows that body mass diminished under the effect of AOH, as compared to base value. Body weight loss increased with increase in duration of the experiment. In the 19-day experiment, the animals lost 700 to 950 g of their original mass. Analysis of the data revealed that there is a correlation between body and muscle mass, which presented some difficulties in comparing the numerical data obtained for both experimental and control animals with different base body mass. Difficulty of analysis was also aggravated by the presence of individual differences in degree of muscle development in the monkeys and, furthermore, by the small number of animals used. Nevertheless, if we compare the weight of homologous muscles in monkeys with approximately the same weight at the start of the experiment, or if we take into consideration the difference in base weight of experimental and control animals, it can be determined that muscle mass remains virtually unchanged with 7-day hypokinesia, whereas with

19-day hypokinesia the decrease in body weight is associated with loss of muscle mass. It could be assumed that, under hypokinetic conditions, the mass of the gastrocnemius, which is one of the main antigravity muscles, would decrease more than that of the brachial biceps, since the anterior extremities were not immobilized and could move actively. However, the mass of these muscles decreased to about the same extent.

Parameters characterizing condition of monkey's skeletal muscles

| Animal group | Animal No | Base weight, g | Weight after experim., kg | Soleus | | | |
|--------------|-----------|----------------|---------------------------|---------|------------------|------------|-----------------------------------|
| | | | | mass, g | muscle fiber CSA | | capillaries per 500 muscle fibers |
| | | | | | red | inter-med. | |
| Control | 1 | 3,000 | 3,200 | 4,500 | 2.0 | 2.8 | 231 |
| | 2 | 3,250 | 3,400 | 6,700 | 2.5 | 3.7 | 273 |
| | 3 | 3,750 | 3,800 | 6,500 | 3.2 | 4.2 | 229 |
| AOH 7 days | 4 | 3,300 | 3,100 | 5,000 | 2.0 | 3.6 | 216 |
| | 5 | 3,300 | 3,300 | 6,450 | 3.2 | 5.6 | 213 |
| AOH 19 days | 6 | 4,450 | 3,500 | 5,500 | 1.6 | 2.1 | 207 |
| | 7 | 3,800 | 3,100 | 4,300 | 1.6 | 2.6 | 189 |
| | 8 | 3,600 | 2,800 | 4,000 | 1.6 | 2.4 | 212 |

| Animal group | Gastrocnemius | | | | | Brachial biceps | | | | |
|--------------|---------------|------------------|-------|------------|--------------------------|-----------------|------------------|-------|------------|--------------------------|
| | mass, g | muscle fiber CSA | | | capil/ 500 muscle fibers | mass, g | muscle fiber CSA | | | capil/ 500 muscle fibers |
| | | red | white | Inter-med. | | | red | white | inter-med. | |
| Control | 17,050 | 2.3 | 4.4 | 2.9 | 183 | 11,500 | 2.6 | 4.4 | 3.2 | 191 |
| | 18,400 | 2.8 | 4.4 | 3.1 | 236 | 12,700 | 2.1 | 3.8 | 2.7 | 181 |
| | 22,200 | 2.1 | 4.0 | 2.0 | 263 | 15,700 | 2.7 | 6.3 | 4.0 | 244 |
| AOH 7 days | 20,600 | 1.5 | 3.6 | 2.0 | 226 | 12,200 | 2.6 | 4.9 | 3.4 | 219 |
| | 20,200 | 2.2 | 4.4 | 2.9 | 215 | 11,750 | 2.3 | 3.2 | 2.6 | 182 |
| AOH 19 days | 20,550 | 1.5 | 3.4 | 2.3 | 231 | 12,400 | 2.0 | 4.1 | 2.8 | 232 |
| | 16,400 | 1.0 | 2.1 | 1.5 | 92 | 12,600 | 2.1 | 4.0 | 2.9 | 200 |
| | 17,700 | 1.6 | 4.0 | 1.8 | 152 | 12,500 | 2.0 | 4.7 | 3.1 | 203 |

The results of the morphometric studies revealed that the drop in muscle mass is due to reduction in diameter of muscle fibers, so that we can discuss development of an atrophic process in the muscles. This process was the most marked in red fibers of the gastrocnemius and soleus. In spite of the seemingly substantial loss of muscle mass, the weight drop, which ranged from 18.5 to 22.5%, can apparently not be attributed solely to muscular atrophy. It is also necessary to consider the fact that, with AOH, there is considerable dehydration of the body [9], and under the influence of the stressor reaction that is usually associated with hypokinesia, there is mobilization of fat from reservoirs.

Some difficulties arose in evaluating data obtained when counting functional capillaries in view of the considerable variability of their number in homologous muscles of control animals. The impression is gained that, with increase in

weight of the animal, the number of functional capillaries in muscles increases. Yet, a comparison of number of functional capillaries in muscles of experimental and control monkeys who had approximately the same base weight obviously shows that their number decreases in all three of the muscles examined during AOH, but to different degrees in different muscles. The changes were less marked in the soleus and brachial biceps than in the gastrocnemius.

Thus, in spite of the fact that redistribution of blood and its accumulation in the upper part of the trunk occurred in the monkeys, no signs of such redistribution were demonstrable in muscles of the animals' limbs (both upper and lower) at the microcirculation level. Evidently, the reduction in number of functional capillaries is a common occurrence in muscles where an atrophic process develops as a result of diminished function. A similar finding was made in animals, in which muscular atrophy occurred after removal of static load in weightlessness [10] and in denervation experiments [11, 12].

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STRUCTURAL DISTINCTIONS OF THYROID C CELLS AND PARATHYROID GLANDS OF PRIMATES DURING HEAD-DOWN HYPOKINESIA

Moscow KOSMICHESKAYA BIOLOGIYA I AVIAKOSMICHESKAYA MEDITSINA in Russian Vol 18, No 2, Mar-Apr 84 (manuscript received 17 Jan 83) pp 73-77

[Article by G. I. Plakhuta-Plakutina, Ye. A. Savina, N. P. Dmitriyeva, Ye. A. Amirkhanyan, G. S. Belkaniya and D. S. Tavadyan]

[English abstract from source] Eight monkeys *Macaca rhesus* were exposed to head-down tilt for 7 days and to clinostatic hypokinesia for 7 days with subsequent 12-day head-down tilt. C cells of the thyroid gland and the parathyroid glands of 5 control and 8 experimental monkeys were investigated histologically, morphometrically and electron-microscopically. On the 7th tilt day the C cell population increased, their nuclei grew significantly, synthesis activated, and secretory granules accumulated. By day 19 most C cells were in the secretion stage. Morphological signs of an increased functional activity of the thyroid gland were seen on experimental day 7 and those of the parathyroid gland on day 19, both in light and electron microscopies. Taking into account the antagonism of C cells and parathyroid glands, it can be assumed that the hypocalciemic effect of calcitonin plays a part in the stimulation of parathyroid glands during head-down tilt.

[Text] Disturbances in the hormonal element of control of calcium metabolism are constantly observed during spaceflights, as well as with various forms of hypokinesia, in animals and man. More recently, there has been considerable heightening of interest in such studies on primates, in view of the similarity of metabolic processes in them and man. Regulation of blood calcium level is similar in man and monkeys [1, 2]. Changes in mineral metabolism, increased resorption of bone tissue in long bones and thinning of cortical layer were observed in the cases of a week-long spaceflight and 2-month or longer immobilization of monkeys [3-6].

A substantial role is attributed to thyroid and parathyroid hormones in maintaining calcium homeostasis. However, morphological studies of these glands associated with extreme factors such as immobilization, clinostatic and antiorthostatic [head tilted down] hypokinesia (AOH) are covered only in isolated works.

Methods

Experiments with AOH were conducted at the Sukhuml vivarium of the Institute of Experimental Pathology and Therapy, USSR Academy of Medical Sciences. *Macaca rhesus* monkeys (males) 3-5 years of age served as the material for our study. A special method of immobilizing the animals in horizontal position [9] was used to create hypokinesia. The tests with AOH at an angle of -6° for 7 days were performed on 2 monkeys; in a 19-day experiment, the animals (6 monkeys) were submitted to clinostatic hypokinesia for 7 days, then in head-down position, at an angle of -6° , for 12 days. As a control, we used five monkeys kept in open-air cages.

A special study was made of C cells of the thyroid and the parathyroid glands using histological, morphometric methods and electron microscopy [8].

Results and Discussion

The thyroid and C cells of intact primates were described in a previous report [8]. As it was shown, primate C cells are distinctly demonstrable only with use of special techniques, in particular, impregnation of sections according to Grandi. They are localized primarily in the central part of the gland and they resemble those of man in distribution in tissue (parafoollicular and epifoallicular), as well as in structural distinctions [10, 11]. Electron microscopy revealed that there are 1-3 C cells with a round nucleus, fine nucleoli and accumulation of nuclear substance under the membrane in the foallicular wall near the basal margin in control specimens. A clear hyaloplasm and presence of small, round, osmiophilic secretory granules are typical features of these cells. There is a moderate quantity of granules; the mitochondria are fine, with compact matrix; the granular endoplasmic reticulum (GER) is arranged in the form of short and narrow cisternae and blebs throughout the cytoplasm.

With 7-day AOH, there is distinct increase in functional activity of both the thyroid and C cell system. The latter form large accumulations in parafoallicular tissue and epifoallicular region, along the basal margin of the foallicles. There is prevalence of large parafoallicular cells with many secretory granules; less degranulated forms are encountered less often (Figure 1a). The population of C cells increases by 42%, as compared to the control. The C-cell nuclei are 26% larger than in the control (see Table). Electron microscopy of experimental specimens revealed that C cells were also encountered considerably more often, and they were larger than in the control (4-5 cells per foallicle). They were characterized by hyperplasia of cell organelles: well-developed Golgi complex, numerous mitochondria, considerable number (up to 17) of GER cisternae, specific secretory granules formed large accumulations in cytoplasm.

With 12-day AOH (following 7-day hypokinesia) signs of thyroid hypofunction developed in most monkeys. In this experiment, most C cells presented different stages of degranulation (Figure 1b). In three out of six experimental monkeys (young, impuberal specimens) there was prevalence of large cells with loose distribution of granules in cytoplasm and degranulated forms. As on the 7th day of the experiment, the nuclei of their C cells remained enlarged (by 27%, as compared to the control). In contrast, in three other, more grown specimens, the size of parafoallicular cell nuclei did not differ distinctly from the control.

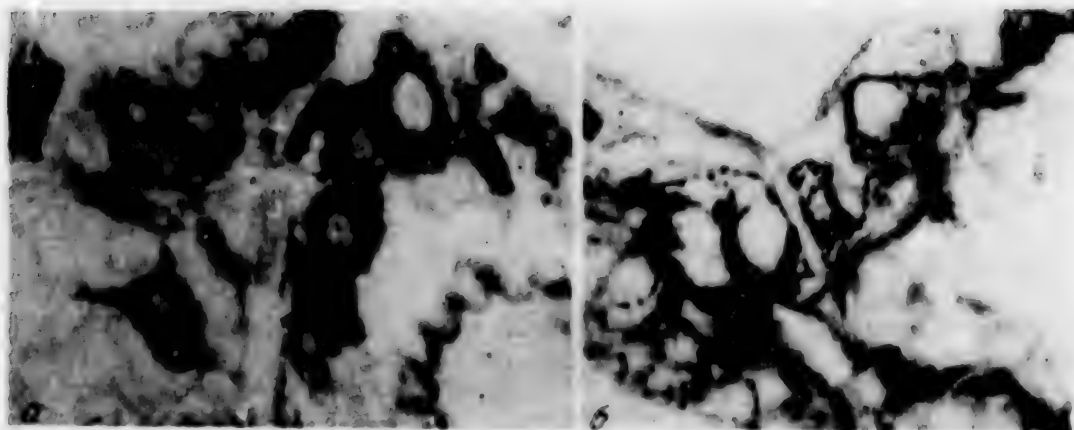


Figure 1. Condition of thyroid C cells during head-down hypokinesia

- a) 7th day; considerable accumulation of secretory granules in C-cell cytoplasm; Grandi method, magnification 600×
- b) 19th day of AOH, C cells are at different stages of degranulation; Grandi method, 600×

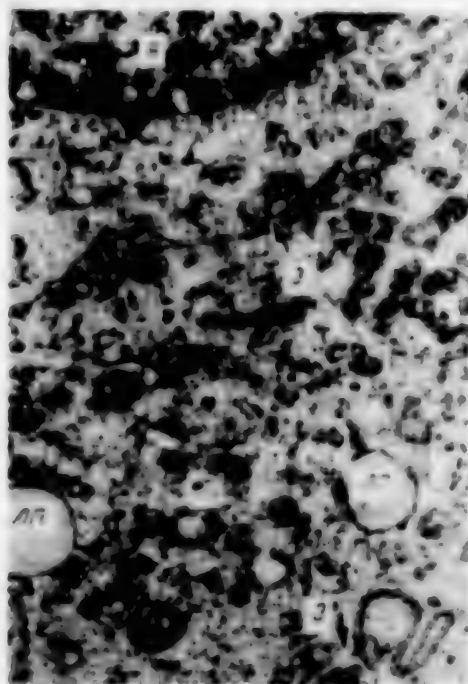


Figure 2.
Primate parathyroid gland.
Control: intricate "locks"
(z) on cell border, lipid drop-
lets (n); n--nucleus;
magnification 20,000×

The reduction in quantity of C cells to the control level (see Table) could be attributed, to some extent, to degranulation signs, since it is not possible to identify all cells (they are poorly outlined) at this stage of the secretory cycle. For this reason, it is difficult to count such cells, and the count reflects only the part of the cell population containing granules.

Morphometric parameters of C cells and parathyrocytes of monkeys submitted to head-down hypokinesia for different times (7 and 12 days)

| Time of study | C cells (per field of vis.) | Nucleus volume, μm^3 | |
|------------------|----------------------------------|-----------------------------------|-----------------------------------|
| | | C cells | parathyrocytes |
| Control | 4.7 ± 0.4 | 110.0 ± 4.8 | 106.3 ± 2.8 |
| After 7-day AOH | 6.7 ± 0.4 ($P < 0.02$) | 139.3 ± 6.4 ($P < 0.02$) | 117.7 ± 6.3 ($P = 0.05$) |
| After 19-day AOH | 5.0 ± 0.16 ($P > 0.05$) | 140.4 ± 8.5 ($P < 0.02$) | 124.4 ± 2.9 ($P < 0.01$) |

*7-day clinostatic hypokinesia followed by 12-day AOH.

The parenchyma of parathyroid glands of control monkeys is represented mainly by a population of clear chief parathyrocytes that are rather similar in shape and size. Parathyrocytes form rosettes of 6-8 cells, their cytoplasm is compact with fine granules. Electron microscopy also revealed prevalence of clear parathyrocytes; the margins of the cells form intricate "locks" and the intercellular space is narrow. The nuclei are of an irregular shape with aggregated chromatin. In the cytoplasm, GER is represented by 3-4 parallel narrow cisterns, the mitochondria are scattered over the cytoplasm, they are fine, most often elongated with a moderately compact matrix, and they occasionally form accumulations. Some lipid droplets are encountered (Figure 2).

On the 7th and 19th experimental days, more marked polymorphism of cells was demonstrated in the parathyroid glands, as compared to the control, i.e., along with light parathyrocytes which made up most of the gland, dark and oxiphilic ones were encountered. The typical features also include enlargement of parathyroid itself (in 2 monkeys on the 19th experimental day), capillary plethora and focal hypertrophy of parathyrocytes manifested by enlargement of nuclei and nucleoli, and clearing of cytoplasm. Karyometric studies revealed that there was only a tendency toward enlargement of parathyrocyte nuclei by the 7th day; by the 19th day their size increased appreciably (see Table), and the parathyroid of young monkeys reacted the most similarly.

Electron microscopy showed that the boundaries of parathyrocytes become more even, the number of complicated "locks" decreases and dilated intercellular spaces with microvilli are often encountered (Figure 3). In clear chief cells, GER is situated above the nucleus in the form of 5-7 parallel, narrow cisternae; there are many polysomes in the cytoplasm in the form of rosettes (see Figure 3a); accumulations of mitochondria are encountered, which are either round or elongated, with densely packed parallel cristae and osmophilic matrix (see Figure 3b). There are few lysosomes, occasionally with

lipid inclusions. The nucleus is round, with aggregated or diffuse distribution of chromatin; the nucleolus is most often near the inner membrane of the nucleus. GER in dark chief cells is arranged in concentric circles, which occasionally form myelinoid bodies. Centrioles are encountered in the clear chief cells (see Figure 3a). A large number of mitochondria in cytoplasm is a typical feature of oxyphilic cells. The mitochondria are round, with sparse matrix and irregularly arranged cristae. Many capillaries similar in structure to control specimens are demonstrable in the parathyroid parenchyma.

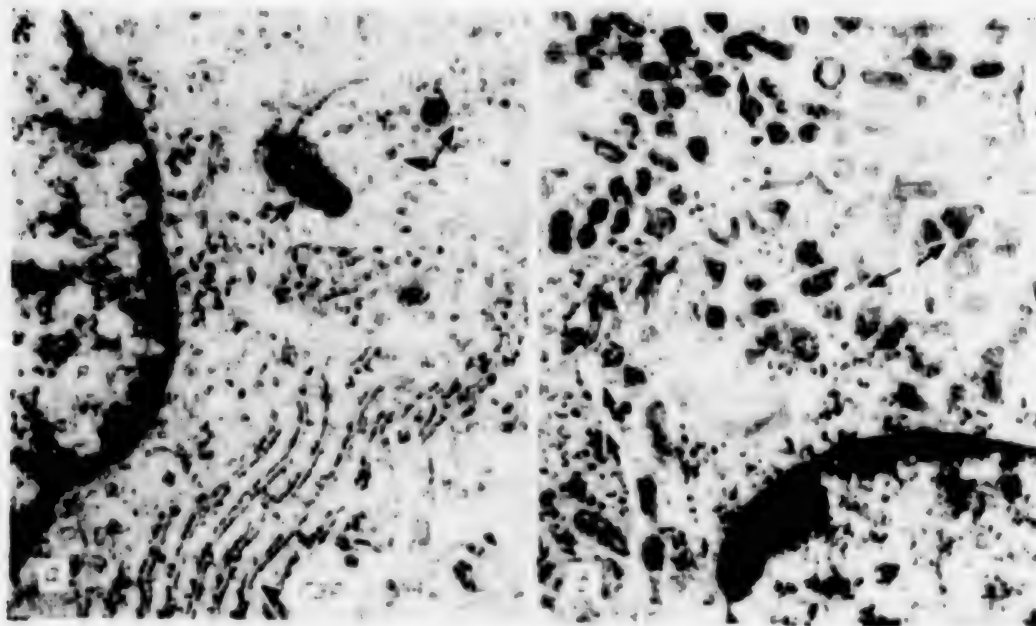


Figure 3. Parathyroid gland, magnification 20,000x

19th day of AOH; numerous polysome (*nc*) rosettes seen in cytoplasm on the left; enlarged GER cysternae (*U*--centriole, *x*--nucleus); on the right there are dilated intercellular spaces; accumulation of mitochondria (*M*) in cytoplasm

The above data indicate that the reaction of thyroid C cells, as well as parathyroid glands depends on duration of AOH.

Analysis of reactive changes in the system of C cells revealed that, in the 7- and 19-day experiments, there are morphological signs of intensification of their functional activity. With 7-day AOH, there is prevalence of signs of increased synthesis with accumulation of secretory granules, whereas on the 19th day most cells are at the stage of releasing secretions. Intensification of functional cells that produce calcitonin could be related to a stressor reaction due, in particular, to immobilization, which leads to substantial increase in TKT [thyrocalcitonin?] activity in blood [12], or change in blood calcium level which, as we know, rises during bedrest and other forms of hypokinesia.

On both the light and ultrastructural levels, the parathyroid glands showed signs of intensification of parathyrocyte activity on the 7th and, particularly, 19th days of the experiment. While there was only a tendency toward enlargement of their nuclei by the 7th day of AOH, nucleus volume was reliably increased by the 19th day. A comparison of the dynamics of structural changes in C cells and parathyroid glands revealed that parathyrocyte activity appears somewhat later than that of C cells. Considering the antagonism between parathyroid glands and C cells, it can be assumed that stimulation of the parathyroid is due to the hypocalcemic effect of calcitonin.

The results of the morphological studies of primate parathyroid glands with AOH are consistent with data in the literature. In humans, prolonged hypokinesia and AOH (182 days) elicited a substantial (by more than 2 times) increase in parathyroid hormone in blood by the 26th day [13].

Thus, the morphological changes in the thyroparathyroid complex, in the form of activation of parathyroid glands and C cell system, are indicative of involvement of this hormonal factor in regulation of calcium metabolism of primates under the effect of AOH.

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METHODS

UDC: 616.2-008.87-034.-07

METHOD OF DETERMINING INTENSITY OF ELIMINATION OF MICROORGANISMS FROM HUMAN UPPER RESPIRATORY TRACT

Moscow KOSMICHESKAYA BIOLOGIYA I AVIAKOSMICHESKAYA MEDITSINA in Russian Vol 18, No 2, Mar-Apr 84 (manuscript received 26 Apr 83) pp 78-80

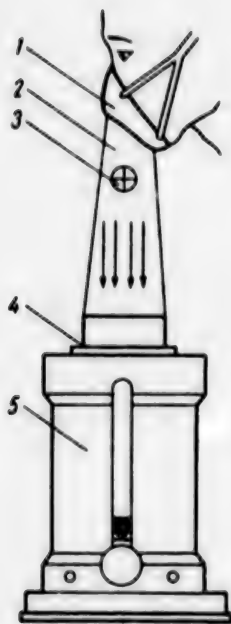
[Article by G. O. Pozharskiy]

[Text] We know of about 200 nosological diseases with an air- and droplet-borne mechanism of transmission of infection. The role of carriers of pathogens of a number of infectious diseases with such mechanism of their transmission through air is unquestionable [1]. The stage of elimination of pathogens of infectious diseases from the human upper respiratory tract into the environment is one of the chief ones in the mechanism of air-borne transmission of infection [2, 3]. At the present time, staphylococcal infections hold a special place among such diseases [4-7]. The existing methods of investigation, such as demonstration of carriers of pathogenic staphylococci in the upper respiratory tract [8, 9], do not reflect the quantitative evaluation of elimination of these microorganisms into the environment, and consequently they do not permit assessment of the epidemiological significance of a carrier. It is thus necessary to develop new methods of studying the distribution of pathogenic staphylococci [10-12] and steps aimed at preventing infections where the pathogens are transmitted by a droplet mechanism.

Methods

The method of determining intensity of exhalation of microorganisms from the human upper respiratory tract is based on the principle of forced aspiration of air exhaled during articulation.

As shown in the Figure, aspiration of exhaled air is effected with an attachment consisting of mask 1, air duct 2, in the upper third of which valve 3 is installed, and ring fastener 4, with which the attachment is connected to the air collecting part of Krotov's apparatus 5. The air duct may be made of transparent polyethylene film. The subject (see Figure) reads aloud a standard text for 4 min. Krotov's apparatus is turned on with the start of articulation, and air is collected at the rate of 25 l/min. This permits complete aspiration of the entire volume of exhaled air [11] on solid nutrient medium in a Petri dish placed in the apparatus. With intake of air in inspiration, valve 3 opens and air passes through the air duct into the subject's upper respiratory tract. In inspiration phase, valve 3 closes and exhaled air is aspirated on the dish with nutrient medium in the Krotov apparatus.



Attachment for Krotov apparatus to determine intensity of output of microorganisms from human upper respiratory track in flow of exhaled air

- 1) mask
- 2) air duct
- 3) valve
- 4) fastening ring
- 5) Krotov apparatus

For comparative evaluation of the proposed method, in the course of the study we also used the method of cultivating microorganisms from the upper respiratory tract during direct articulation in Petri dishes.

In this case, the subject read a standard text for 4 min, and an open Petri dish with solid nutrient medium was placed 15 cm in front of his mouth [12, 13].

We used solid nutrient media in these studies: 5% blood, yolk-salt and mannitol-salt agars. After collecting the microflora, the dishes with 5% blood and yolk-salt agars were incubated for 2 days at a temperature of 37°C, after which the colonies were counted. The dishes with mannitol-salt agar were placed in anaerostats and incubated at 37°C for 5 days, after which we counted and isolated the staphylococcal strains that decompose mannitol and determined the capacity of these microorganisms to coagulate plasma. The isolated strains were typed using an international set of phages.

We tested three groups. The first consisted of 4 essentially healthy men, each of whom was tested 10 times. We used 5% blood agar. We determined the intensity of elimination of total number of microorganisms from the upper respiratory tract, as well as

quantity of staphylococci with the property of hemolyzing erythrocytes.

The second group consisted of 4 essentially healthy people who were carriers of staphylococci with positive lecithinase activity. In all of these subjects, staphylococci that had the above reaction were demonstrable in the range of $2 \cdot 10^2$ – $2 \cdot 10^5$ in the buccal cavity and $1.6 \cdot 10^2$ – $2 \cdot 10^5$ on the mucosa of the anterior parts of the nasal passages. We used as nutrient medium egg yolk-salt agar in order to count staphylococci with positive lecithinase reaction. Each subject in this group was tested by this method five times.

The medical personnel of a surgical department made up the third group (13 people). The purpose of this study was to determine the intensity of their elimination of pathogenic staphylococci into the environment. We determined the size of the bacterial focus formed by pathogenic staphylococci on the mucosa of the anterior nasal passages. In these tests we used mannitol-salt agar.

Results and Discussion

As shown by the results of these studies, which are listed in Table 1, total quantity of microorganisms isolated from the flow of exhaled air by means

of the attachment and Krotov apparatus exceeded significantly, other conditions being equal, the number demonstrated by direct articulation on a Petri dish. This pattern was also noted when we counted hemolytically active staphylococci. Control studies of microorganisms in the air of the room in which the tests were performed showed that there were reliably fewer than in the flow of exhaled air assayed with the attachment and Krotov apparatus. The results listed in Table 2 demonstrate the advantages of the proposed method, as compared to the known method used for determination of intensity of elimination of staphylococci with lecithinase activity from the upper respiratory tract of individuals, in whose mouth and mucosa of anterior segments of nasal passages these microorganisms were found. During the control tests, no staphylococci with lecithinase activity were demonstrable in the air of the room, in which the tests were performed.

Table 1. Evaluation of efficacy of methods of determining total quantity of microorganisms in flow of air exhaled by essentially healthy people

| Indicator | Articulation directly on open Petri dish with nutrient medium for 4 min (10 tests) | P ₁ | Articulation with use of attachment and Krotov apparatus for 4 min (10 tests) | P ₂ | Microorganisms per 100 l room air (collected in 4 min with Krotov apparatus; 10 tests) |
|---------------------------------------|--|----------------|---|----------------|--|
| Total number of microorganisms | 28±10 | 0.001 | 70±10 | 0.05 | 43±5 |
| Breakdown: | | | | | |
| staphylococci with hemolytic activity | 17±3 | 0.001 | 40±4 | 0.02 | 15±3 |
| staph. without hemolytic activity | 10±2 | 0.05 | 24±4 | 0.5 | 20±2 |
| Gram-negative bacilli | " " | -- | 2±1 | -- | 5±2 |
| Gram-positive " | 1±0.5 | -- | None | -- | 5±2 |

Key: P₁) reliability of differences as compared to method of articulating directly on open Petri dish

P₂) same as compared to results of demonstrating microorganisms in room air

The results of examining surgical department medical personnel for demonstration and evaluation of intensity of output of pathogenic staphylococci from the upper respiratory tract into the environment are listed in Table 3. They showed that the proposed method, with use of solid mannitol-salt agar, made it possible to determine the activity of elimination of pathogenic staphylococci from the upper respiratory tract of some employees.

These results are indicative of the fact that a bacterial focus is not demonstrable by simply taking a smear from the mucosa of the anterior segments of the nasal passage with a sponge, and this does not indicate that there is no

output of pathogenic staphylococci in the flow of exhaled air. Evidently, the above phenomenon is attributable to colonization of these microorganisms on the mucous membranes of the parts of the nose from which it is impossible to take smears with a sponge, as well as probable presence of these microorganisms in the buccal cavity.

Table 2. Comparative evaluation of efficacy of methods of determining quantity of staphylococci with lecithinase activity in flow of air exhaled by carriers of these microorganisms

| Tested carrier | Direct articulation on open Petri dish with nutrient med. for 4 min(5 tests) | | Articulation with attachment and Krotov apparatus for 4 min(5 tests) | | Staphylococci/100 l room air (collected for 4 min with Krotov apparatus(5 tests) | |
|----------------|--|------|--|-------|--|------|
| | 1 | 2 | 1 | 2 | 1 | 2 |
| B-v | 8±2 | None | 26±6 | 1±0.3 | 21±4 | None |
| P-v | 12±4 | • • | 27±14 | 4±3 | 20±3 | • • |
| I-v | 7±1 | • • | 20±6 | 9±3 | 22±4 | • • |
| Zh-v | 10±1 | • • | 30±7 | 7±1.5 | 18±3 | • • |

Key: 1) total number of staphylococci
2) quantity of staphylococci with positive lecithinase activity

Table 3. Evaluation of intensity of elimination of pathogenic staphylococci in flow of air exhaled by medical personnel, as determined with attachment and Krotov apparatus

| Tested carrier | Staph. concentration in exhaled flow during articulation (per 100 l air, 4-min articulation) | | | Size and features of focus formed by pathogenic staph. (anterior nasal mucosa) | | Staph. concentration in room air (taken for 4 min; 100 l air) | |
|----------------|--|------|-------|--|----------------------------------|---|------|
| | 1 | 2 | 3 | 1 | 2 | 1 | 2 |
| I-va | 31 | None | None | 6·10 ⁵ | Not typed with international set | 25 | None |
| P-v | 34 | 20 | 80/52 | 8·10 ³ | 80/52 | 30 | • • |
| Zh-va | 47 | 7 | 29/85 | None | None | 35 | • • |

Key: 1) total number of staphylococci
2) staphylococci that decompose mannitol and coagulate plasma
3) staphylococcus phage types

Thus, a new method of determining the intensity of output of pathogenic microorganisms, in particular pathogenic staphylococci, from the human upper respiratory tract into the environment has been developed and evaluated with a positive result.

This method can be used to elaborate preventive measures aimed at control of pathogens of infectious diseases that spread through the air.

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BRIEF REPORTS

UDC: 616.153.1:577.152.199]+616.36-008.
931:577.152.199]-02:629.78]-092.9

OXIDATIVE ENZYME ACTIVITY IN RAT BLOOD PLASMA AND SUBCELLULAR FRACTION OF LIVER FOLLOWING FLIGHT ABOARD COSMOS-936 BIOSATELLITE

Moscow KOSMICHESKAYA BIOLOGIYA I AVIAKOSMICHESKAYA MEDITSINA in Russian Vol 18, No 2, Mar-Apr 84 (manuscript received 1 Mar 83) pp 81-82

[Article by R. A. Tigranyan and Ye. G. Vetrova]

[Text] Experiments simulating the effect of weightlessness on man and animals (water immersion, hypokinesia), as well as during long-term manned spaceflights, revealed changes in activity of enzymes of oxidative metabolism in blood serum, as well as in subcellular fractions of rat liver and myocardium [1-4].

Our objective here was to investigate the activity of the key enzymes of oxidative metabolism--malate dehydrogenase (MDH) and isocitrate dehydrogenase (ICDH)--in rat blood plasma and subcellular liver fractions after completion of flight aboard Cosmos-936 biosatellite. The Krebs cycle is the general ultimate route of oxidative catabolism of protein, fats and carbohydrates in living organisms. The activity of different reactions of the Krebs cycle as a whole determines the intensity of oxidative processes in tissues. NAD-dependent MDH and NADP-dependent ICDH play a substantial part in this sequence of reactions; both the overall rate of conversion of substrates in the cycle and ratio of oxidized to reduced forms of coenzymes (NAD and NADP) in cytoplasm and mitochondria depend on the activity of these enzymes. The reaction catalyzed by ICDH is also used in ancillary biosynthetic reactions of the cycle. Thus, the study of MDH and ICDH is of substantial relevance to evaluation of energy metabolism in rat tissues.

Methods

The studies were pursued with male Wistar SPF (Bratislava, CSSR) rats, flown for 18.5 days in space aboard Cosmos-936 biosatellite. The characteristics of experimental conditions and designations of animal groups were furnished previously [5]. The mitochondrial and cytoplasmic fractions were isolated from a liver homogenate by centrifuging at 4500 G for 30 min. The mitochondrial fraction, which was submitted to dialysis against 0.01 M tris-HCl, pH 7.8, for 1.5 h, the cytoplasmic fraction and blood plasma were used to measure activity of MDH [6] and ICDH [7]. Concentration of protein was assayed by the method in [8].

Results and Discussion

A comparison of MDH and ICDH activity in blood plasma of rats flown aboard the biosatellite and submitted to weightlessness or artificial gravity (AG) failed to demonstrate changes either in parameters of the above mentioned flight groups or in comparison to values for vivarium control animals. The parameters of both groups of rats in the synchronous experiments also failed to reveal changes in activity of the tested enzymes, as compared to the vivarium control (Tables 1 and 2).

Table 1.

MDH activity in blood plasma (NADH/ml/min), in cytoplasmic and mitochondrial fractions (NADH/mg protein/min) of rat liver ($M \pm m$)

| Rat Group | Blood plasma | Cytopl. fraction | Mitoch. fraction |
|-----------------------------|--------------|------------------|------------------|
| VK ₁ | 491 ± 31,9 | 6457 ± 381 | 4657 ± 466 |
| FW ₁ | 515 ± 109,7 | 5325 ± 310,5* | 4448 ± 670 |
| FC ₁ | 459 ± 118,6 | 5347 ± 255,5* | 4954 ± 988 |
| SW ₁ | 481 ± 86,4 | 7792 ± 600 | 3521 ± 277 |
| SC ₁ | 476 ± 87,0 | 7399 ± 602 | 4396 ± 529 |
| C ₁ ⁰ | 499 ± 41,1 | 6114 ± 1173 | 4504 ± 1436 |
| VK ₃ | 616 ± 73,1 | 8516 ± 146 | 4663 ± 380 |
| FW ₃ | 495 ± 48,7 | 8387 ± 687 | 5013 ± 389 |
| FC ₂ | 558 ± 46,5 | 9686 ± 514 | 5208 ± 181 |
| SW ₃ | 520 ± 104,5 | 9292 ± 1205 | 4854 ± 278 |
| C ₂ ⁰ | 564 ± 85,3 | 7194 ± 781 | 6178 ± 1712 |

* $P < 0,05$.

Table 2.

ICDH activity in blood plasma (NADP/ml/min) in cytoplasmic and mitochondrial fractions (NADP/mg protein/min) of rat liver ($M \pm m$)

| Rat group | Blood plasma | Cytopl. fraction | Mitoch. fraction |
|-----------------------------|--------------|------------------|------------------|
| VK ₁ | 13,4 ± 2,7 | 317 ± 27,2 | 84,7 ± 7,1 |
| FW ₁ | 13,1 ± 1,8 | 226 ± 37,0* | 81,2 ± 6,9 |
| FC ₁ | 13,7 ± 6,9 | 260 ± 19,9 | 88,5 ± 12,3 |
| SW ₁ | 16,8 ± 3,0 | 352 ± 32,1 | 99,5 ± 33,7 |
| SC ₁ | 10,8 ± 1,4 | 304 ± 24,0 | 80,7 ± 6,7 |
| C ₁ ⁰ | 9,8 ± 1,1 | 302 ± 37,9 | 92,0 ± 21,3 |
| VK ₃ | 14,4 ± 1,84 | 429 ± 60,5 | 90 ± 15,0 |
| FW ₃ | 11,6 ± 1,5 | 451 ± 47,4 | 124 ± 8,1 |
| FC ₂ | 10,5 ± 1,1 | 495 ± 20,5 | 123 ± 16,5 |
| SW ₃ | 12,2 ± 1,42 | 493 ± 34,5 | 114 ± 11,1 |
| C ₂ ⁰ | 12,6 ± 1,9 | 426 ± 20,3 | 143 ± 38,3 |

* $P < 0,05$.

Key for both tables:

- VK) vivarium control
- FW) flight group in weightlessness
- FC) flight group with artificial gravity (centrifuge)
- SW) synchronous ground-based experiment in weightlessness
- SC) synchronous ground-based experiment with artificial gravity
- C) centrifuge (artificial gravity)

Examination of MDH and ICDH activity in rat liver mitochondrial fraction also failed to demonstrate changes in activity of these enzymes, in either the two flight groups or animals in synchronous control, as compared to parameters for rats in the vivarium control (see Tables 1 and 2).

Testing of MDH in the cytoplasmic liver fraction immediately after landing revealed a reliable decrease (by 18%) in MDH activity in flight animals, and this decline was noted both in rats in weightlessness and AG (see Table 1). ICDH activity decreased less significantly, and the differences were reliable only in rats submitted to weightlessness (see Table 2). It should be noted that the decrease in MDH and ICDH activity was reliable in comparison to parameters for animals of both the vivarium control and synchronous experiment.

With regard to MDH and ICDH activity in ground-based SC₁ and C₁⁰ groups, we found some unreliable increase in MDH activity in the cytoplasmic fraction with no change in ICDH level (see Tables 1 and 2).

The demonstrated decrease in activity of the tested enzymes in both flight groups of rats and absence of analogous changes in animals of the synchronous control may apparently be indicative of the fact that the decrease in MDH and ICDH activity is attributable to the specific effect of spaceflight factors. In addition, the absence of differences in enzyme activity in rats that were weightless during the flight and in those submitted to AG indicates that use of AG does not eliminate the specific effect of weightlessness on activity of the tested enzymes. It can be assumed that, under the effect of spaceflight factors, the intensity of oxidative processes in the rat liver does not undergo appreciable changes, since activity of mitochondrial MDH and ICDH does not differ from the control level. The decrease in MDH and ICDH activity in the cytoplasmic fraction, however, could lead to a change in correlation between oxidized and reduced forms of NAD and NADP within the mitochondria and in the cytoplasm of liver cells, which could be interpreted as one of the possible mechanisms of controlling the intensity of such important processes in hepatic cytoplasm as glycolysis and gluconeogenesis.

The increase in MDH activity in the cytoplasmic fraction of the liver of rats in the synchronous experiment could be attributed to the fact that animals in this group were perhaps subject to stressors of greater strength than the flight groups. This is confirmed by the findings of increased MDH activity in rat liver under the influence of increased secretion of steroid hormones (in particular, cortisol) under the effect of stressors [9].

We observed normalization of MDH activity in the cytoplasmic fraction of the liver in flight groups and synchronous experimental groups of animals 25 days after the flight, as compared to parameters for the vivarium control. However, activity of MDH and ICDH in the cytoplasmic and mitochondrial fractions of animals in all groups was somewhat higher than in those tested immediately after termination of the experiment. It can be assumed that this increase in activity of oxidative enzymes is due to the manipulations performed on these animals during the recovery period.

Thus, the demonstrated changes in activity of enzymes of oxidative metabolism, which were due to the effects of spaceflight factors, were reversible and reverted to normal 25 days after conclusion of the experiment.

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EFFECT OF CENTRIFUGING ON SURVIVAL OF EARLY LARVAE OF COMMON FROGS

Moscow KOSMICHESKAYA BIOLOGIYA I AVIAKOSMICHESKAYA MEDITSINA in Russian Vol 18, No 2, Mar-Apr 84 (manuscript received 17 Feb 83) pp 82-84

[Article by E. A. Oygenblik]

[Text] It is known that there are periods sensitive to hypergravity, but reactions of the developing embryo to prolonged and relatively mild exposure to it had not been investigated before, and there are no data that would enable us to evaluate the regulatory capacity of embryos submitted to this factor.

Our objective here was to test the effect of accelerations of 2, 3 and 5 G on survival of embryos and early larvae of the common frog [*Rana temporaria*] and incidence of developmental anomalies.

Methods

Experiments were conducted with eggs collected during the spawning season from water reservoirs in the vicinity of the Zvenigorod Biological Station of Moscow State University. We used two identical BMTs-1 miniature biological centrifuges which generated accelerations of 2 to 5 G. There were 6 250-ml beakers in each centrifuge. This enabled us to conduct experiments on eggs from six clutches simultaneously. We collected clutches from the water no more than 30 min after fertilization. In the laboratory we took 3 samples of 200-400 eggs each from each clutch. One sample served as a control and the other two were placed in the centrifuge beakers. Thus, each experiment (Table 1) consisted of 18 series. We began all of the tests at the gray falcula stage. In the 1st-5th experiments, the material was submitted to the same accelerations in both centrifuges to different stages of development. In the 1st-3d experiments, the eggs developed to the blastula stage on one centrifuge and gastrula on the other. In the 4th and 5th experiments, they were centrifuged past the third groove and to the gastrula stage; in the 6th experiment, the eggs developed at accelerations of 3 and 5 G to the neurula stage. The developmental stages were tracked according to the control.

Immediately after exposure to accelerations, part of the material from each experimental series was examined with a binocular in order to detect developmental abnormalities. After inspections, the eggs were returned to trays, in which they were to develop until they hatched. During mass hatching, we counted

normal and deformed larvae, eggs that perished in embryogenesis, as well as larvae that perished after hatching.

Results and Discussion

The results of our counts are listed in Tables 2-4.

Table 1.
Protocol of experiments

| Experi- m No | Inten- sity, G | Stage at which exposure was stopped | Expo- sure time, h |
|--------------------|----------------------|--|-----------------------------|
| 1 | 5 | Gastrula | 24 |
| | | Blastula | 18 |
| 2 | 3 | Gastrula | 24 |
| | | Blastula | 18 |
| 3 | 2 | Gastrula | 24 |
| | | Blastula | 18 |
| 4 | 5 | Gastrula | 24 |
| | | 3d groove | 5 |
| 5 | 2 | Gastrula | 24 |
| | | 3d groove | 5 |
| 6 | 5 | Neurula | 46 |
| | 3 | | |

As can be seen in Table 2, accelerations of 2 and 3 G to the blastula and gastrula stages did not reliably increase either overall or embryonic death. Overall death refers to the number of embryos that died during embryogenesis and after hatching. Accelerations of 2 G also failed to have an appreciable effect on onset of developmental anomalies. However, with 3 G there was a tendency toward increase in number of embryos that developed abnormally. The effect of 5 G accelerations was much more devastating for frog embryos. There was some increase in deaths at the embryonic stages, but to a lesser extent than after hatching. The increase in deaths after hatching was statistically

reliable. There was also a reliable increase in number of abnormal larvae, both among those that continued to develop and those that perished. A comparison to the control revealed that the anomalies were not referable to eggs with diminished viability, but those that were viable. Examination of the material showed that abnormal embryos continued to develop until the uncoordination of morphogenetic processes led to death.

Table 2. Effect of centrifuging to blastula and gastrula stages on development of frog embryos ($\bar{X} \pm m$)

| Experi- m No | Exposed to | Stage | Overall deaths % | Death at embryonic stages | Abnormal larvae, % | | |
|--------------------|---------------|----------|------------------------|---------------------------------|--------------------|-----------------|---------------|
| | | | | | dead | develop- ing | total |
| 1 | 5g | Gastrula | 34.18 ± 10.9 | 24.75 ± 9.01 | 9.43 ± 2.29* | 11.38 ± 2.29* | 20.81 ± 3.34* |
| | | Blastula | 36.13 ± 10.38 | 25.72 ± 7.56 | 10.41 ± 3.73* | 7.77 ± 1.16 | 6.54 ± 2.92 |
| | | Control | 14.54 ± 5.57 | 14.54 ± 5.57 | 0 | 0 | 0 |
| 2 | 3g | Gastrula | 7.17 ± 2.80 | 5.67 ± 1.83 | 1.56 ± 1.16 | 2.93 ± 2.36 | 4.49 ± 3.46 |
| | | Blastula | 4.91 ± 1.64 | 4.20 ± 1.08 | 0.73 ± 1.21 | 6.15 ± 4.58 | 6.88 ± 5.8 |
| | | Control | 4.51 ± 1.31 | 3.48 ± 0.48 | 1.02 ± 1.00 | 0.98 ± 0.91 | 2.00 ± 1.98 |
| 3 | 2g | Gastrula | 9.88 ± 3.76 | 8.02 ± 3.39 | 1.85 ± 0.98 | 1.05 ± 0.81 | 2.90 ± 0.97 |
| | | Blastula | 9.13 ± 2.30 | 7.37 ± 1.66 | 1.65 ± 1.32 | 0.59 ± 0.59 | 2.24 ± 1.91 |
| | | Control | 6.77 ± 1.84 | 6.77 ± 1.84 | 0 | 0 | 0 |

* $P < 0.01$

Table 3. Effect of centrifuging to third groove and gastrula on development of frog embryos ($\bar{X} \pm m$)

| Exper. No | Exposed to | Stage | Overall deaths % | Death at embryonic stages % | Abnormal larvae, % | | |
|-----------|------------|-----------|-------------------|-----------------------------|---------------------|-----------------|------------------|
| | | | | | died after hatching | developing | total |
| 4 | 5 g | Gastrula | 41.71 \pm 11.68 | 22.70 \pm 6.06 | 19.00 \pm 6.11 | 6.63 \pm 1.34 | 25.63 \pm 6.86 |
| | | 3d groove | 18.72 \pm 2.53 | 18.47 \pm 2.51 | 0.24 \pm 0.24 | 0.73 \pm 0.47 | 0.97 \pm 0.67 |
| | | Control | 19.00 \pm 5.70 | 19.00 \pm 5.70 | 0 | 0 | 0 |
| 5 | 2 g | Gastrula | 19.88 \pm 3.70 | 12.31 \pm 2.88 | 7.57 \pm 1.45 | 0 | 7.57 \pm 1.45 |
| | | 3d groove | 15.42 \pm 3.19 | 9.11 \pm 2.43 | 6.30 \pm 1.44 | 0 | 6.30 \pm 1.44 |
| | | Control | 15.93 \pm 1.68 | 13.46 \pm 5.14 | 2.47 \pm 1.19 | 0 | 2.47 \pm 1.19 |

Table 4. Effect of centrifuging to neurula on development of frog embryos ($\bar{X} \pm m$)

| Experiment No | Exposed to | Overall deaths % | Death at embryonic stages, % | Abnormal larvae, % | | |
|---------------|------------|-------------------|------------------------------|---------------------|-------------------|-------------------|
| | | | | died after hatching | developing | total |
| 6 | 5 g | 75.64 \pm 6.55* | 41.62 \pm 10.04 | 34.21 \pm 8.14* | 11.06 \pm 2.98* | 35.27 \pm 9.36* |
| | 3 g | 29.91 \pm 7.80 | 16.42 \pm 5.57 | 16.42 \pm 5.57 | 13.49 \pm 2.24 | 21.37 \pm 3.81* |
| Control | | 24.59 \pm 4.03 | 17.01 \pm 3.91 | 7.58 \pm 1.24 | 0.14 \pm 0.13 | 7.72 \pm 1.27 |

* $P < 0.01$.

The experiments with centrifuging of eggs from the same clutches to the third groove and to the gastrula stage were conducted in order to see the effect on development on the borderline between the second and third periods of high sensitivity (see Table 3). The data obtained with centrifuging at accelerations of 2 and 5 G to the gastrula stage in these tests conform well to the results of the preceding experiments. Eggs submitted to centrifuging at acceleration of 5 G to the third groove showed virtually no difference from the control; however, exposure to 2 G to the same stage increased somewhat the death rate after hatching, although this was statistically unreliable. The high sensitivity of eggs in the experiments of this series, which were submitted to milder centrifuging, is attributable to individual distinctions of the clutches exposed in this experiment, rather than to increased sensitivity to a milder factor.

Centrifuging to the neurula stage was used on eggs from the same clutches, but with different levels of accelerations (see Table 4). We found that such prolonged exposure to 5 G accelerations reliably increased overall death rate and number of abnormal larvae (both live and dead), and it elicited a significant

increase in deaths at embryonic stages. Accelerations of 3 G used up to the neurula stage are much milder, but there was a reliable increase in number of live anomalous larvae, with appearance of a distinct trend toward more deaths after hatching.

If we compare the results of exposure to accelerations of 3 and 5 G to the gastrula and neurula stages, it becomes apparent that centrifuging to the latter stage elicits more anomalies and deaths at different stages of development. This is a somewhat unexpected finding, since it is believed that amphibian embryos are sensitive to changes in gravity only up to the gastrula stage. However, it was found that there is yet another period of high sensitivity of embryonic development to increased gravity, the period from the middle gastrula to neurula stage. The limits of this period will be defined in future experiments.

NUCLEIC ACID CONTENT OF CANINE LIVER DURING LONG-TERM EXPERIMENTAL HYPOKINESIA

Moscow KOSMICHESKAYA BIOLOGIYA I AVIAKOSMICHESKAYA MEDITSINA in Russian Vol 18, No 2, Mar-Apr 84 (manuscript received 25 Dec 82) pp 85-86

[Article by V. G. Prisenko]

[Text] Many researchers are interested in the biochemical mechanisms of adaptation of different organs and tissues to extreme factors [1-5]. It is known that adaptation of the body to difficult environmental situations is based on activation of nucleic acid and protein synthesis [6].

Our objective here was to investigate the quantitative levels of nucleic acids in animal liver cells in the case of prolonged restriction of mobility (from 24 h to 240 days).

Methods

We examined the liver of 24 dogs of the same weight (9-11 kg), which were kept in "hypokinetic" chambers, i.e., special dog cages [7]. Quantitative assay of nucleic acids in liver cells was made by the method of R. G. Tsanev and G. G. Markov [8]. Before measuring nucleic acids, the liver was perfused with saline, the tissue was frozen at -20°C temperature, after which a homogenate of liver cells was obtained, which was centrifuged under refrigeration at 10,000 r/min for 30 min. We homogenized 100 mg hepatic tissue in 10% trichloroacetic acid under refrigeration. The residue after removal of acid-soluble compounds was dried in an incubator at 37°C . Nucleic acids were extracted from the residue with 1 N HClO_4 . Absorption in the ultraviolet region was measured by a spectrophotometric method using a Specord UV-VIC spectrophotometer at wavelengths of 260 and 286 nm for RNA, 263 and 284 nm for DNA. All of the data were calculated in milligrams of P per 100 mg fresh tissue.

As a control, we studied 5 dogs, and average characteristics of quantitative levels of DNA and RNA in liver cells were determined, which are in the range of 30 and 80 mg% P, respectively.

The mean results are listed in the Table.

Dynamics of nucleic acid levels in canine liver cells over 240-period of hypokinesia (M±m)

| Duration of hypokines. | Number of dogs | Liver | |
|------------------------|----------------|------------|------------|
| | | DNA, mg% P | RNA, mg% P |
| 24 h | 2 | 29.9±5.0 | 75.2±4.2 |
| 3 days | 3 | 28.4±2.5 | 65.0±5.0 |
| 10 " | 2 | 29.2±3.0 | 64.4±3.6 |
| 30 " | 3 | 27.8±2.6 | 49.4±4.3 |
| 90 " | 3 | 10.4±2.2 | 25.4±4.0 |
| 180 " | 3 | 11.2±1.8 | 22.3±2.0 |
| 240 " | 3 | 10.8±1.7 | 24.4±5.2 |
| Control | 5 | 30.4±4.2 | 79.0±3.8 |

Results and Discussion

Nucleic acid content in canine liver cells under hypokinetic conditions does not change appreciably for up to 30 days, there being only a tendency toward decrease in RNA, as compared to DNA, particularly toward the end of a month of restricted movement.

A general and drastic decrease in nucleic acid content of liver tissues was observed after 3 experimental months. At this stage, there is apparently utilization of the naturally accumulated pool of amino acids, with impairment of systemic metabolic processes. Cases have been described in the literature of diminished protein synthesis in the rat myocardium during

100-day hypokinesia, and of total free amino acids in skeletal muscles on the 45th-60th days of restricted movement [7].

After 6 and 8 months of hypokinesia, the quantity of nucleic acids in liver cells becomes stable; it remains virtually the same as with 3-month hypokinesia.

The data we obtained about reduction in nucleic acid content of liver cells with 90-day hypokinesia conform with data submitted in the literature, and they can apparently be indicative of diminished activity of processes of protein and nucleic acid metabolism in general, if we consider the fact that processes of protein biosynthesis take place mainly in the liver.

Thus, the results of biochemical analysis indicate that long-term hypokinesia leads to reduction in quantity of nucleic acids in the liver. The critical period of restricted movement has been established--3 months--when the nucleic acids have minimum values, as compared to normal; further hypokinesia does not lead to decline in liver cells, which is consistent with data we published previously [9].

In our opinion, in the presence of weightlessness and under clinical conditions, one should pay special attention to hypokinesia lasting 30 to 90 days, since this period is apparently the one of the most substantial metabolic changes in the body.

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INFLUENCE OF EXAM STRESS ON CARDIAC FUNCTION OF STUDENTS DIFFERING IN
LEVEL OF PHYSICAL ACTIVITY

Moscow KOSMICHESKAYA BIOLOGIYA I AVIAKOSMICHESKAYA MEDITSINA in Russian Vol 18,
No 2, Mar-Apr 84 (manuscript received 28 May 82) pp 86-87

[Article by N. Ya. Volkind]

[Text] A high degree of motor activity increases man's resistance to stressors, improves central nervous system (CNS) function, diminishes fatigue, improves endurance during prolonged mental work, enhances immunobiological properties, resistance to diseases, improves heat-regulating mechanisms, etc. [1-6].

Conversely, prolonged hypokinesia elicits adverse changes in the human body: it diminishes myocardial contractility [7], adaptive and compensatory capacities of the body [7-8], causes drastic changes in hormone and mediator metabolism [9], alters trophics [10], causes marked asthenization [8-10], etc. Emotional reactivity changes drastically under such conditions [11].

We studied some parameters of cardiac function during final exams in students, athletes and unconditioned subjects.

Methods

We studied students on the faculty of physical education and faculty of biology and geography. The first group consisted of masters, candidates for master of sports and first-category athletes (25 people) and the second consisted of unconditioned subjects (35). We selected students showing identical achievement to the extent this was possible. Most of the subjects were young men.

We recorded the EKG in the second standard lead, in seated position. Heart rate was calculated from the R-R interval, blood pressure was measured according to Korotkov. EKG parameters and blood pressure recorded on the morning after the exams served as the control. Data for 20 people from each group were submitted to statistical processing. The rest of the information was submitted to visual analysis.

Results and Discussion

The changes in cardiac activity during the exams were different in physically conditioned and unconditioned students. There were moderate functional changes

in the heart of students on the physical education faculty, and they were more marked in biology students (see Table).

Changes in duration of cardiac cycles (R-R intervals) at different stages of exams for students differing in physical activity (n = 20; M±m)

| Exam period | Students | R - R |
|-----------------------------------|----------|-------------|
| Before receiving QC | HCA | 0,808±0,053 |
| | NAS | 0,575±0,044 |
| After receiving QC | HCA | 0,798±0,071 |
| | NAS | 0,568±0,040 |
| Student preparation for answering | HCA | 0,825±0,068 |
| | NAS | 0,28±0,046 |
| At start of answering QC | HCA | 0,692±0,058 |
| | NAS | 0,492±0,026 |
| At end of answering QC | HCA | 0,795±0,065 |
| | NAS | 0,565±0,031 |
| Waiting for grade | HCA | 0,902±0,067 |
| | NAS | 0,618±0,044 |
| After grades are posted | HCA | 0,920±0,069 |
| | NAS | 0,635±0,040 |
| Recovery period | HCA | 0,918±0,066 |
| | NAS | 0,685±0,042 |
| Quiet period | HCA | 1,062±0,042 |
| | NAS | 0,870±0,041 |

Note: QC--question card; HCA--high-class athletes; NAS--nonathletic students; P<0.05.

The amplitude of P waves showed a mild tendency toward increasing. It reached 1.30±0.22, 1.28±0.21, 1.35±0.19, 1.22±0.16 mm before and after receiving the question card, at the start and end of answers, respectively, and was 0.92±0.14 mm at rest. The difference in amplitude between quiet and above exam periods was reliable (P<0.05). The increase in amplitude of this wave is indicative of increased influence of the sympathetic nervous system [12].

Thus, high-ranking athletes are highly resistant to the stress of examinations. This is indicated by the moderate changes in their cardiac activity during the exams. Other researchers have also reported on the beneficial effect of physical conditioning on the heart [13-15].

Unconditioned students presented more marked changes in cardiac activity during exams. These changes, as in the athletes, progressed as the moment of giving answers drew nearer, and they gradually regressed after the students received their grades. These changes were demonstrable for a number of EKG parameters.

In this group of students, R-R intervals were the shortest. Their average pulse rate at the start of giving answers constituted 122.3±2.65/min versus 89.15±7.39/min in the athletes.

We also demonstrated a more marked tendency toward increase in amplitude of P wave in unconditioned students. Before and after receiving the question card, at the start and end of contact between the examiner and student, this

amplitude constituted 1.55 ± 0.20 , 1.50 ± 0.24 , 2.12 ± 0.32 and 1.70 ± 0.24 mm, respectively, with 1.12 ± 0.13 mm at rest. The differences in amplitude between quiet period and important phases of the exam were reliable ($P < 0.05$).

The difference in reactivity of the cardiovascular system of high-ranking athletes and unconditioned students to exam stress was also demonstrable in blood pressure parameters. Thus, while giving answers, athletes' pulse rate was 81.60 ± 6.20 /min, systolic, diastolic and pulse pressure constituted 128.5 ± 4.35 , 81.50 ± 2.64 and 47.75 ± 4.65 mm Hg, respectively; in the quiet period their pulse rate was 56.00 ± 2.50 /min, systolic, diastolic and pulse pressure constituted 108.25 ± 2.87 , 66.75 ± 1.90 and 41.50 ± 1.70 mm Hg, respectively; in unconditioned students, while answering test questions pulse rate was 105.60 ± 7.93 /min, systolic, diastolic and pulse pressure were 131.00 ± 5.13 , 85.50 ± 3.03 and 45.50 ± 3.79 mm Hg; in the quiet period the figures were 72.80 ± 5.77 /min, 110.00 ± 2.74 , 70.25 ± 1.42 and 39.50 ± 1.99 mm Hg. The low pulse pressure is indicative of uneconomical cardiac function.

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MOUSE ADRENAL CORTICOSTERONE CONTENT DURING PROLONGED EXPOSURE TO HIGH-INTENSITY STATIONARY MAGNETIC FIELD

Moscow KOSMICHESKAYA BIOLOGIYA I AVIAKOSMICHESKAYA MEDITSINA in Russian Vol 18, No 2, Mar-Apr 84 (manuscript received 29 Mar 82) pp 87-89

[Article by Z. F. Kuz'mina]

[Text] There are data in the literature indicating involvement of the adrenocortical system in the reaction to a stationary magnetic field (SMF). Signs of increased functional activity of the adrenal cortex were demonstrated by histological and histochemical methods in rats after 30-min exposure to 912 Oe (0.09 T) SMF [1] or 1-3-h exposure to SMF of 4500 Oe (0.45 T) [2]. Repeated exposure (30 min daily for 30 days) to 912 Oe SMF led to decline of adrenocortical function [1]. In mice exposed continuously to SMF of 4200-9000 Oe (0.42-0.9 T), morphological signs of activation of the adrenal cortex persisted for 4-35 days. However, in experiments on rats no changes were demonstrated in corticosterone level of the adrenals and blood plasma after exposure to SMF of 9000 Oe for 3-14 days [3]. An increase in excretion of 17-hydrocorticosteroids in urine was demonstrated in squirrel monkeys for the first 6 days of exposure to SMF of 200 Oe (0.02 T); by the 10th day, in spite of continued exposure, the hormone level in urine did not differ from control values [4].

Our objective here was to evaluate the functional state of the adrenal cortex according to its corticosterone levels in the course of prolonged and continuous exposure to high-intensity SMF.

Methods

Experiments were performed with CBA and C57 B1 hybrid male mice with base weight of 17-22 g. The animals were exposed to whole-body vertically oriented field with induction of 1.6 T. We used an SP-57A electromagnet with pole pieces in the form of a circle with 450-mm radius and 100-mm air gap between tips to generate magnetic fields. The generated magnetic field was strictly stationary and homogeneous in a radius of 380 mm; induction dropped from 1.6 to 1.3 T from this range to the edge of the pole piece. The mice were placed in the gap of the electromagnet in plexiglas cages in the shape of a sector of a circle. Control animals were kept in the same room under analogous conditions, in a phantom of pole pieces made of duralumin. The magnetic was turned off for 30 min daily to clean the cages and feed the animals. The mice were given feed pellets, carrots, cottage cheese and water ad lib.

Three repeated series of experiments at different times of the year: 15-day exposure (May and October) and 30-day exposure (February). Adrenal corticosterone was assayed after exposure to SMF for 1, 4, 10, 15, 22 and 30 days, then 6 days after 30-day exposure. Ten animals from the experimental and 10 from the control group were decapitated simultaneously (always at the same time of day). The adrenals were excised, fatty tissue removed and they were weighed to the closest 0.1 mg. Corticosteroid content was assayed by the fluorometric method of Guillemin et al. [5], as modified by V. M. Rozental' [6].

Results and Discussion

In control mice ($n = 107$), adrenal corticosterone content was $6.2 \pm 0.6 \mu\text{g/g}$. There were noticeable seasonal fluctuations in levels of this hormone. The highest level was observed in the May experiment-- $10.5 \pm 1.0 \mu\text{g/g}$ ($n = 33$). In October, the control level was $4.8 \pm 0.9 \mu\text{g/g}$ ($n = 40$) and in February, $3.8 \pm 0.3 \mu\text{g/g}$ ($n = 34$).

Long-term exposure to SMF with induction of 1.6 T (up to 30 days) had no noticeable effect on the animals' general condition, weight and adrenals (Table 1).

Table 1. Change in weight of body and adrenals of mice under the effect of SMF of 1.6 T

| Exposure time days | Body mass, g | | Adrenals, mg/g body wt. | |
|-----------------------|------------------------|------------------------|---------------------------|---------------------------|
| | control | experiment | control | experiment |
| 1 | 18.9 ± 0.8 (18) | 20.2 ± 0.6 (21) | 0.157 ± 0.008 (18) | 0.166 ± 0.009 (21) |
| 15 | 20.0 ± 0.7 (29) | 23.8 ± 0.9 (27) | 0.147 ± 0.005 (29) | 0.142 ± 0.004 (27) |
| 30 | 30.7 ± 2.4 (7) | 27.6 ± 1.2 (10) | 0.099 ± 0.0017 (7) | 0.089 ± 0.007 (10) |

Note: Here and in Table 2, the number of animals is given in parentheses.

Table 2 sums up the results of assaying corticosterone in mouse adrenals with exposure to SMF for different periods of time. Typical dynamics of change in adrenal corticosterone levels are demonstrable in the course of 30-day exposure to SMF. After 1 day of exposure to SMF, the animals showed a reliable increase in amount of this hormone in the adrenals (to $203.3 \pm 40.9\%$ of the control level). The high corticosterone level persisted after 4 days. By the 10th day it corresponded to control values; it dropped reliably after 15 days, then rose again by the 30th day of exposure in the SMF. Six days after termination of 30-day exposure, adrenal corticosterone content was close to the control level ($120.1 \pm 18.4\%$).

Analysis of the results of the different series of experiments revealed seasonal fluctuations in magnitude of effect of SMF with the same direction of changes in hormone content. The first phase of activation of hormone production was more marked in the May experiment than the October one; adrenal corticosterone

Table 2.
Corticosterone content ($\mu\text{g/g}$) in
mouse adrenals with exposure to
SMF of 1.6 T

| Exposure time, days | Experiment | Control |
|--------------------------|---------------------|---------------------|
| 1 | 9.2 ± 1.4 (21) | 6.5 ± 1.6 (18) |
| 4 | 10.0 ± 3.1 (18) | 6.6 ± 1.3 (17) |
| 10 | 5.6 ± 1.3 (15) | 7.6 ± 1.5 (19) |
| 15 | 4.1 ± 0.6 (27)* | 7.2 ± 1.14 (29) |
| 22 | 3.3 ± 0.4 (10) | 2.7 ± 0.4 (9) |
| 30 | 4.6 ± 0.7 (10)* | 2.8 ± 0.4 (7) |
| 6 days after exposure | 3.2 ± 0.4 (10) | 2.6 ± 0.3 (8) |

* $P < 0.02$.

level rose to 241.3 and 161.4%, respectively. The phase of decline in functional activity of the adrenal cortex was equally marked in May and October (51.9 and 55.5%) and considerably less in February (70.7%).

Consequently, prolonged exposure to high-intensity SMF elicits three phases of changes in mouse adrenal corticosterone content, reflecting its functional state. According to current conceptions, such dynamics of changes in corticosterone are inherent in the reaction of the pituitary-adrenocortical system to diverse stressor agents [7]. These phases occurred within shorter periods of time with strong and brief stressors. SMF is a mild stimulus [8] and, under our experimental conditions, a long-acting one. Evidently, this is why the phases were extended in time. There

are no grounds to view the decrease in corticosterone content of the adrenal on the 15th day of exposure of mice to SMF as a phase of depletion of the adrenocortical system. The repeated though less significant increase in hormone production with continuing exposure to the magnetic field (30th day) speaks against this.

At the present time, the phase of subnormal adrenocortical activity in the course of stress reactions is viewed as a defense that prevents exhaustion of resources of the hypothalamo-hypophyseal-adrenocortical system and limits the effect of corticosteroids on body tissues [7]. The phasic course of the stress reaction is controlled by complex regulatory systems, which include feedback mechanisms, nervous and neurohumoral influences [7, 9-11]. From this point of view, the data on biphasic reaction of the hypothalamo-hypophyseal neurosecretory system are of interest; it develops at the same times as in our experiments, but with considerably less intensive SMF. The phase of activation of neurosecretion was observed for the first 3 days and phase of depression on the 15th day of exposure of rats to SMF of 1000 Oe (0.1 T) [12].

Thus, the reaction of the adrenocortical system to prolonged exposure to a strong magnetic field (1.6 T) is characterized by a specific pattern. The initial intensification of function is followed by adaptation to the continuously present magnetic field, with a phase of diminished hormone synthesis. With further exposure to this factor, there is a second activation of adrenocortical function.

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BOOK REVIEWS

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REVIEW OF BOOK ON SPACE RADIOBIOLOGY

Moscow KOSMICHESKAYA BIOLOGIYA I AVIAKOSMICHESKAYA MEDITSINA in Russian Vol 18, No 2, Mar-Apr 84 (signed to press 15 Feb 84) pp 89-92

[Review by V. V. Antipov and B. I. Davydov of book "Space Radiobiology" by Yu. G. Grigor'yev, Energoizdat, Moscow, 1982, 176 pages]

[Text] Space radiobiology emerged and developed on the basis of general radiobiology, space biology and medicine.

Research on the biological effects of cosmic radiation started in the 1930's and was motivated by the assumption that spontaneous mutations occur in living organisms under the influence of natural ionizing radiations.

From the late 1940's to late 1950's, the attention of researchers was focused mainly on investigation of biological effects of the heavy component of cosmic radiation. This question arose in connection with the problem of assuring radiation safety of manned spaceflights, which were being planned already at that time.

Experiments were conducted on diverse biological systems with use of aircraft, high-altitude and ballistic rockets.

Finally, in the 1960's, radiobiological experiments started to be performed on artificial earth satellites (AES) and manned spacecraft. The main objective of the first flight experiments was to determine the extent of radiation hazard on the planned flight routes for specific types of spacecraft. Experiments were conducted with a broad spectrum of biological systems (from biological preparations to dogs), with use of diverse methods that permitted evaluation of possible radiation damage from the molecular to the organismic levels.

Along with data concerning the physical dose of cosmic radiation, the results of these experiments made it possible to draw a rather important conclusion, that the radiation situation in orbits below earth's radiation belts, with the sun in a calm state, presents no hazard to man on short-term flights aboard Vostok type spacecraft. During the flights made in that period, an effort was made to study the RBE [relative biological effectiveness] of different components of cosmic radiation, the effect of several flight factors and, first of all, weightlessness, on radiation damage, etc. Yu. G. Grigor'yev and his coworkers

have made a substantial contribution to the inception and development of space radiobiology. For several years, they successfully studied the distinctions of biological effects of different types of cosmic radiation, including heavy particles of galactic cosmic radiation. They investigated the modifying influence of weightlessness on the radiobiological effect; they developed approaches to evaluation of radiation safety of short- and long-term manned flights, methods of protection against radiation, etc.

This is the second monograph by Yu. G. Grigor'yev dealing with generalization and analysis of extensive experimental material obtained both on earth and different types of space vehicles. The ultimate purpose of this research was, as we know, to elaborate an effective system of measures to assure the radiation safety of man's flights into space.

The monograph begins with a brief description of the radiation situation in space.

At the present time, there is much information about the physical parameters of ionizing radiation in near-earth space, radiation near the moon and certain other planets of the solar system. However, the author furnishes such information for the purpose of assessing possible irradiation and, consequently, the degree of hazard to crews during short- and long-term spaceflights.

As we know, setting standards for ionizing radiation, evaluation or, more precisely forecasting radiation hazard as related to flight conditions--duration, nature of orbit, degree of protection, etc.--are exceptionally difficult tasks. To solve these problems, development of fundamental theoretical questions dealing, in particular, with general physiological aspects of the patterns of the body's reactions to radiation, as well as experimental studies of the distinctions of biological effects of cosmic radiation and, first of all, its heavy component, are required. These problems make it necessary to answer the equally difficult problems of combined effect on the body of ionizing radiation and flight factors other than radiation.

All these questions have been covered in the monograph under review.

For example, Chapter 2 deals with general physiological conceptions of the body's reaction to ionizing radiation.

Yu. G. Grigor'yev was the first radiobiologist to pay attention to the need for comprehensive investigation and consideration of the role of the CNS [central nervous system] in the body's reaction to radiation in setting standards for radiation burden of cosmonauts.

There are many fundamental data about the effect of radiation on different parts of the CNS in the worldwide and, particular, Soviet radiobiological literature. However, they turned out to be insufficient to solve a number of problems related to setting standards for the radiation factor in relation to long-duration spaceflights.

For this purpose, a chronic experiment was performed on dogs under the supervision of Yu. G. Grigor'yev, with simulation of radiation conditions during long-term spaceflights. At the present time, the obtained data make it possible

to evaluate the immediate effects of a 3-6-year period of exposure to radiation for different annual doses (from 1.25 to 1.88 Gy).

Some of the results of this unique experiment are described in the monograph, and they pertain to different types of disturbances in conditioned reflex activity that dogs develop when chronically exposed to radiation. Thus, after 3 years of continuous exposure to radiation, a decrease in strength and lability of the excitatory process, increased inertia of the inhibitory process, impaired coordination of these processes in the conditioned chain motor reflex, etc., were demonstrated.

Of great interest are the data of this author and his coworkers concerning investigation of compensatory capabilities of the CNS proper after exposure to ionizing radiation, on the model of adaptive biocontrol. This model conforms to closed biological systems, in which the self-regulation element is in the CNS and, consequently, it permits investigation of the system's capacity to control its own activity. The condition of self-regulating intimate CNS processes in an irradiated organism exposed to rather high doses was evaluated for the first time in these experiments.

The general physiological mechanisms of the body's reactions to ionizing radiation, as well as the possibility of strict differentiation between the damaging and stimulating effects of this factor, which are discussed by the author in the same chapter, alter appreciably our conceptions and approaches to evaluation of radiation hazard of spaceflights.

Analysis of the literature and his own data about physiological and behavioral reactions to radiation led to a rather important conclusion: Under the effect of low doses of ionizing radiation one can predict that "radiation stimulation" will not affect performance of motivated assignments; in the case of high doses in a situation with limited or excessive sensory input and when it is necessary to perform complicated tasks, one cannot categorically maintain that the human body will retain adequate and accurate perception and emotional stability. Unfortunately, the author does not discuss questions related to the reaction of the CNS to nonuniform irradiation. Yet there are works in the literature indicative of a substantial difference in behavioral reactions, depending on localization of radiation, and these facts cannot be overlooked in setting standards for or forecasting the outcome of radiation damage, particularly in emergency situations (powerful solar flare and others).

Chapter 3 assesses the combined effect of ionizing radiation and other physical environmental factors. The author explores on a modern theoretical level the possible mechanisms of the body's reactions to a combination of environmental factors; he cites some interesting material of his own about radioresistance of the body in the case of prior exposure to stationary and electromagnetic fields, hypoxia, etc. The sections in which analysis is made of the link between the body's radiosensitivity and its biorhythms, with discussion of questions of forecasting the effects of combined physical environmental factors, also merit attention.

The author validly observes that the problem of combined effect of factors is one of the basic problems of space biology and medicine.

At the present time, there are quite a few works dealing with the problem of combined effects of spaceflight factors. However, most of them are descriptive, and the studies were made in order to learn about the qualitative changes that arise under the combined effect of factors with regard to the different parameters. At the same time, there have been few studies to establish the quantitative patterns of the body's reactions to a set of factors or mathematical description of general biological patterns when body reactivity changes under these conditions. It is quite apparent that it is impossible to predict biological, including radiobiological, effects of combinations of different factors and, in essence, it is impossible to scientifically validate spaceflight factor standards without solving these problems.

It had been reported in many of our works that there are several objective reasons limiting research on this subject. They include the absence of general theory to describe the basic principles of interaction of the body with the set of factors to which it is exposed simultaneously or successively, the shortage of models of interaction of factors of both theoretical and great practical interest to the support of manned flights. The flaws include also the unsatisfactory use of mathematical methods in most studies, in particular, multifactor variance analysis in planning experiments, analyzing results and their use to set standards for factors.

In the light of the foregoing, the data in this monograph dealing with the combined effect on the body of environmental factors, including those related to spaceflights, enrich our knowledge substantially, both theoretically and in solving specific problems associated with multifactor experiments. We wish to praise, in particular, the author's attempt at considering the problem of the body's responses to a number of physical environmental factors and ionizing radiation from the standpoint of triggering adaptive mechanisms. At the same time, as correctly stressed by the author, one cannot fail to take into consideration the specific effects related to concrete mechanisms of reactions due to tropism of the factor involved for a given biological system.

Chapter 4 submits data from studies of constitutional radiosensitivity during spaceflights.

As we know, the problem of assessing the modifying influence of spaceflight factors on the radiobiological effect is being studied in ground-based laboratory experiments and in flight. There are various methodological approaches to solving the problem in flight experiments: irradiation of biological objects before spaceflights or after them, launching biosatellites during a solar flare or in earth's radiation belts, irradiating biological objects in space on a specified program, with use of emitters aboard spacecraft or artificial earth satellites.

The organizationally simplest experiments are those involving preflight and postflight irradiation of biological objects that are exposed on satellites that are inserted into orbits below earth's radiation belts during periods of solar calm. In such experiments, there are vast opportunities to vary irradiation conditions, make a differentiated analysis of the effects of the set of nonradiation factors on different stages of formation and development of radiation sickness; they are relatively inexpensive.

However, all of the foregoing pertains mainly to experiments with, for example, bacteria or dry seeds, i.e., biological material that does not require a complicated inflight life-support system. This is why most of the data on the modifying influence of spaceflight factors on the radiation effect were obtained specifically on air-dried seeds of different plants. The first experiments of this kind were conducted in 1961-1963 by N. L. Delone et al., and an attempt was made there to assess the influence of nonradiation factors on the radiobiological effect in the case of short-term (up to 5 days) flights. In these experiments there was brief weightlessness.

The team headed by Yu. G. Grigor'yev conducted a series of studies of the role of weightlessness and its duration in the modifying influence of the set of nonradiation spaceflight factors on the radiobiological effect. Of great value in this respect are, for example, the data obtained by L. V. Nevzgodina et al. for irradiated air-dried salad seeds in an experiment aboard the Salyut station, the flight of which lasted, as we know, 73 days. Unique data were obtained by L. V. Nevzgodina and L. T. Miller et al. in an experiment with salad seeds aboard the Cosmos-782 satellite, which carried a functioning centrifuge. In this experiment, it was possible to test the influence of normal gravity and weightlessness during a spaceflight on formation of the radiobiological effect.

Analysis of numerous data in the literature and those obtained by Yu. G. Grigor'yev concerning preflight and postflight irradiation of plants enabled him to conclude that, although they do have a modifying influence on the radiation reaction, spaceflight factors have an insignificant effect that is not reliably demonstrable in all experiments and, mainly, a stable correlation is not obtained in these tests between the recorded modifying effects and duration of weightlessness.

No doubt, this conclusion motivated performance of experiments with inflight irradiation of biological systems.

In the history of space radiobiology, there have been 4 biological experiments with emitters aboard a spacecraft or artificial earth satellite (these were the relatively simple experiments with blood in vitro aboard Gemini-3, leukocytes and mold aboard Gemini-11 with use of β -applicators onboard) and 2 rather complicated experiments aboard Biosatellite-2 and Cosmos-690.

The experiment performed aboard Cosmos-690 biosatellite by a large team of researchers headed by Yu. G. Grigor'yev was very important from the standpoint of obtaining information about changes in radiosensitivity of animals (rats) and distinctions of formation of radiation lesion with exposure to the combination of ionizing radiation and weightlessness in an actual spaceflight. Such data were obtained for the first time.

The monograph describes comprehensively and analyzes the results of this major and complex investigation, including physiological, biochemical, hematological, clinical and pathomorphological material.

In this experiment, as in those with preflight and postflight irradiation of biological objects, the modifying effect of the set of nonradiation spaceflight factors, including weightlessness, was not large. According to different parameters referable mainly to critical radiosensitive organs, the coefficient of modifying effect is close to 1.0 and does not exceed 1.2.

It can also be concluded that irradiation during a spaceflight can modify a number of reactions of an organism that are specific to weightlessness. We refer, for example, to the effect of weightlessness on cell mitosis (N. L. Delone et al.).

Unquestionably, identification of the modifying influence of actual spaceflight conditions on the radiobiological effect is a step forward in assessing the radiation hazard of spaceflights, and this is a major achievement of the Soviet school of radiobiologists.

Investigation of the distinctions of biological effects of different types of cosmic radiation is one of the most pressing tasks for space radiobiology. At the present time, it has been reliably established that equal doses of absorbed energy from ionizing radiations of different types do not necessarily elicit an identical biological effect, and this must be taken into consideration, in particular when setting standards for cosmonaut exposure to radiation.

Of greatest interest in this regard are the studies of biological effects of heavy nuclei of galactic cosmic radiation. In such experiments, it is particularly difficult to select methods and biological systems for adequate evaluation of the effects in question.

For this purpose, the author and his coworkers developed and used specialized "Bioblock" and "Biostack" assemblies in flight. They made it possible to identify each ion passing through biological systems (*Arabidopsis* seeds, *Artemia salina* eggs, etc.). The results of these studies are submitted in Chapter 5 of the monograph. They indicate that it is necessary to continue studying this complex problem.

Also of great interest are the sections of the chapter, in which the author explores the possible mechanisms of onset of light flashes in cosmonauts under the influence of ionizing radiation and makes a prognostic evaluation of the effect of heavy ions on the nervous system.

In conclusion, it should be noted that the monograph being reviewed contains many new and interesting facts that enrich general and space radiobiology. It submits several original theoretical theses, that are very necessary to scientific validation of standards, with respect to levels of radiation to which cosmonauts are exposed, particularly in long-duration flights. The reader will find much of interest and benefit in the description of methodological procedures, specific instruments used by the author and his colleagues in performing complicated radiobiological studies.

The monograph is well-illustrated, it is easy and interesting to read. No doubt, it is of great interest to radiobiologists and other specialists working in the area of providing for radiation safety of manned spaceflights.

NEW BOOK ON METABOLISM UNDER HYPODYNAMIC CONDITIONS

Moscow KOSMICHESKAYA BIOLOGIYA I AVIAKOSMICHESKAYA MEDITSINA in Russian Vol 18, No 2, Mar-Apr 84 (signed to press 15 Feb 84) pp 92-94

[Review by Ye. A. Kovalenko and Yu. I. Kondrat'yev of book "Metabolism Under Hypodynamic Conditions" by I. V. Fedorov, Izdatel'stvo Nauka, Moscow, 1982, 254 pages]

[Text] The monograph by I. V. Fedorov, "Metabolism Under Hypodynamic Conditions," which was published as part of the series entitled "Problems of Space Biology..." (Vol 44), is a fundamental work summarizing the results of more than 15 years of investigations by the author and the group he heads dealing with metabolism in animals during experimental hypodynamia. For the first time, this book has gathered together and analyzed data on changes in protein, carbohydrate, nucleic and fluid-electrolyte metabolism, as well as their regulatory systems in the case of prolonged restriction of movement. What is valuable is that the author did not limit himself to a statement and enumeration of metabolic disturbances, but examines their order and mutual determination, which enabled him to expound the hypothesis of biochemical bases of pathogenesis of the hypodynamic syndrome. In addition to data obtained from studies of animal metabolism, material is submitted on the influence of hypodynamia on humans, including spaceflight conditions. The experiments with animals are valuable in that they permit investigation of tissue metabolism proper on different levels.

The relevance of the monograph and novelty of material in it are unquestionable. Hypodynamia is widespread among all categories of urban residents. There has been a drastic increase in number of specialists, for whom hypodynamia is becoming a distinctive occupational hazard. There is a large contingent of patients who are compelled to spend a long time on strict bedrest. Investigation of hypodynamia in space medicine occupies a special place.

The book has 11 chapters, a conclusion and bibliography.

Chapter 1 shows the influence of hypodynamia on function of the cardiovascular, respiratory, nervous, muscular systems and other functions of the body. In the subsequent study of metabolism proper, it is not considered apart, but against the background of functional changes in the body and in connection with them.

The next chapter describes experimental models of hypodynamia of rats which were used by the author. It also offers a brief description of many other models. Special chairs, bedrest, immersion in fluid and small chambers are used in studies of the effect of hypodynamia on man. In a number of studies, in addition to rats, primates, dogs, rabbits, birds and even fish served as objects for investigation of hypodynamia.

The author includes changes in weight of the body and different organs among integral indicators of metabolism (Chapter 3). Numerous data are submitted concerning changes in weight of animals and man, which were obtained by the author or taken from the literature. As a rule, in animals hypodynamia leads to loss of weight of the body and different organs, particularly the skeletal muscles. In man, there are more often changes in proportion of protein and fat mass, the latter increases and the former decreases.

The influence of hypodynamia on protein metabolism has been examined the most thoroughly (Chapter 4); in rats, against a background of polyuria, there was significant increase in excretion of total nitrogen, urea, uric acid, creatinine and creatine in urine. There was the same orientation of excretion of nitrogenous components in humans for the first weeks of immobilization. A negative nitrogen balance was usually observed in animals and man. The author demonstrated convincingly in numerous variants of original experiments with radioamino acids that there is noticeable depression of tissue protein synthesis under hypodynamic conditions and faster breakdown thereof. These changes are the most vivid in skeletal muscles. There is a change in quantitative and qualitative amino acid composition of tissues, with decline in levels of functionally active proteins due to increase in share of connective tissue proteins, specifically collagen.

Nucleic metabolism (Chapter 5) has been little-studied. DNA and RNA content per unit tissue mass does not change. There are changes in rate of metabolism, in particular of messenger RNA and in nucleotide composition of RNA.

The changes in carbohydrate metabolism (Chapter 6) in immobilized animals are characterized by persistent hypoglycemia, drastic reduction of tissular glycogen content with concurrent increase in amount of products of its breakdown. The intensity of glycogenolysis diminishes after a certain increase. There is particularly noticeable impairment of the process of oxidative phosphorylation and ATP production.

In animals, lipid metabolism disturbances (Chapter 7) are manifested by a drop of triglyceride levels in tissues with concurrent elevation of cholesterol. There is intensification of lipolytic breakdown of fats, and there is noticeable increase in nonesterified fatty acids, cholesterol and acetone bodies in blood. The same orientation of changes in lipid metabolism, according to several parameters, was demonstrated in man under hypodynamic conditions, in the presence of experimental atherosclerosis and atherosclerosis.

It was shown that the existing data about activity of tissue enzymes (Chapter 8) are sparse and contradictory. Activity of oxidative enzymes and levels of substrates of the Krebs cycle were studied for the first time in the author's laboratory. A significant decrease in activity of oxidative enzymes of the

tricarboxylic acid cycle was demonstrated in contractile tissues with a block in the cycle at the level of isocitrate dehydrogenase.

The section of the monograph dealing with hormones (Chapter 9) is of definite interest. The author analyzed numerous studies on hormone activity and synthesis in animals and man. It was demonstrated that changes in many hormonal parameters of man and rats are in different directions. In a number of cases, an increase in adrenal and pituitary hormone activity was noted, that is inherent in the effect of stress stimuli, and decrease in activity of some anabolic hormones.

Change in fluid-electrolyte metabolism (Chapter 10) is one of the typical reactions to immobilization. The author successfully summarized the data from numerous works about fluid metabolism and electrolyte metabolism. Hypodynamia is characterized by redistribution of body fluids in the direction of decrease in their extracellular share and more intensive elimination of sodium, potassium and, particularly, calcium salts. In some instances, there is a deficiency of these elements in tissues and a negative balance. The author discusses the possible effects of impaired phosphorus and calcium metabolism on body functions.

In the last chapter (Chapter 11) there is brief discussion of recovery from metabolic disturbances following long-term hypodynamia. It is validly noted that this question, which is important to practice, still requires thorough and comprehensive investigation. The recovery period following strict hypodynamia, which equals the entire duration of immobilization, does not always lead to normalization of all metabolic parameters. Prolonged hypodynamia per se elicits a profound change in metabolism and regulatory processes. In the recovery period, the abrupt change from immobilization to unrestricted activity is, in turn, instrumental in a second disruption of regulatory processes.

The last section of the book, the conclusion, is very interesting and unique, and it is based on vast factual material and data in the literature. Referring to a wide range of sources, a thorough analysis was made of the possible causes of decreased protein synthesis under the influence of hypodynamia. The leading role of depression of the transcription process during protein synthesis is demonstrated convincingly. This thesis is reinforced by direct experimental data and several indirect indicators. A comprehensive study was made of the causes and sequence of changes in carbohydrate and fat metabolism. The significance of hypodynamia proper and stress factors it induces on metabolism was demonstrated. Validated original schemes of pathogenesis of changes in protein, fat and carbohydrate metabolism are submitted as the logical outcome of analysis of the material. The author discusses the possible role of changes in microcirculation, peroxidation of lipids and hormonal disturbances in the development of hypodynamic metabolic disorders. The role of hypodynamia is discussed as one of the risk factors in development of cardiovascular diseases.

The monograph ends with a meticulously prepared bibliography listing over 700 titles of works by Soviet and foreign authors.

The book of I. V. Fedorov is the first extensive summarization of results of studying metabolism under hypodynamic conditions. Of course, not all aspects of this problem have been studied deeply enough as yet.

In particular, it would have been of definite interest to discuss extensively questions of calcium metabolism under hypodynamic conditions, the possible role in these conditions of the protein, calmodulin, as well as cyclic nucleotides.

The monograph is unquestionably of great interest, not only to specialists in space biology and medicine, but for clinicians, biochemists, physiologists and other specialists concerned with problems of hypodynamia.

OBITUARY OF NATAL'YA DMITRIYEVNA ZAVALOVA

Moscow KOSMICHESKAYA BIOLOGIYA I AVIAKOSMICHESKAYA MEDITSINA in Russian Vol 18, No 2, Mar-Apr 84 (signed to press 15 Feb 84) pp 94-95

[Article by editorial board]

[Text] Natal'ya Dmitriyevna Zavalova, doctor of psychological sciences, passed away on 30 August 1983 after a serious illness. Soviet aviation psychology and medicine have lost a talented scientist, one of the pioneers in Soviet aviation engineering psychology, who devoted many years to the study of problems of improving the efficiency of flight work and assuring flight safety.

Since 1957, the scientific biography of N. D. Zavalova is inseparably linked with solving the most pressing problems of aviation psychology and medicine. Natal'ya Dmitriyevna started her work in aviation with a painstaking study of the psychological content of pilot work; she participated personally in experiments aboard an aircraft laboratory. Her deep understanding of the specifics of flight work provided vital relevance to the scientific projects of N. D. Zavalova. She devoted much time and effort to investigation of the distinctions of pilot behavior in critical inflight situations. The research done under her supervision and with her direct participation made it possible to formulate scientifically validated principles of construction of emergency signaling systems, including a verbal one, as well as to develop special procedures for training flight personnel for action in critical situations. The solution of complicated problems of assuring the reliability of pilot actions when using automatic aircraft control systems is linked with the work of N. D. Zavalova. The conception of "active operator," which gained wide recognition both in our country and abroad, became an important theoretical generalization of this work.

N. D. Zavalova was one of the initiators of using the systems approach to analysis of erroneous actions of operators. Creative development of systems methodology made it possible to add to the dictionary of aviation psychology and medicine the term, "human factor," to designate errors that occur due to failure to consider the psychological patterns of interaction between operator and machines.

In recent years, investigation of the mental image as a regulator of pilot actions occupied a special place in the scientific creativity of N. D. Zavalova. It was shown in several original works that it is only in the presence of an integral and differentiated mental image that a high degree of reliability of operator performance is achieved. The basic theses of the conception of

regulatory role of mental image were successfully applied in the practice of pilot training.



The fruitful scientific endeavors of N. D. Zavalova were reflected in her numerous scientific works, more than 200 publications, including 3 monographs. She was thoroughly proficient in the art of performing a strict and demonstrative experiment, and was armed with an arsenal of procedures for processing experimental data. The scientific works of N. D. Zavalova were characterized by a clear and convincing style of presentation.

N. D. Zavalova devoted much effort to the training of highly qualified scientific personnel. Several dissertations and theses were defended under her guidance.

Natal'ya Dmitriyevna was active

in public and scientific work; she was a member of a specialized council at the Institute of Psychology, USSR Academy of Sciences; she was a member of the editorial board of our journal; she participated actively in the selection and review of scientific publications, displaying high principles and benevolence in this work.

For her conscientious work, communist N. D. Zavalova received the Honorary Decoration Order.

N. D. Zavalova was always concerned about introduction of her scientific research into practice. She was well-informed about the living and working conditions of pilots, who had a sincere respect for her.

Natal'ya Dmitriyevna Zavalova will always remain in the memory of her comrades and students as an example of infinite devotion to science, high principles, responsiveness and charm.

ABSTRACTS OF ARTICLES FILED WITH THE ALL-UNION SCIENTIFIC RESEARCH INSTITUTE
OF MEDICAL AND MEDICOTECHNICAL INFORMATION

Moscow KOSMICHESKAYA BIOLOGIYA I AVIAKOSMICHESKAYA MEDITSINA in Russian Vol 18,
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FORMATION OF GAS BUBBLES IN GELATINOUS MEDIA IN THE PRESENCE OF DECOMPRESSION

[Abstract of article by Yu. Ya. Kislyakov, Yu. I. Luchakov and S. V. Korovkina]

[Text] Physical properties of gases and decompression conditions affect the nature of distribution of gas bubbles in different tissues. Studies were conducted on a physical model of biological tissues--gelatin of different concentrations at different ambient temperatures--to analyze the effect of physical factors on the number of bubbles under different decompression conditions. The experiments were performed on gelatin samples from the same batch in order to minimize the margin of error due to natural fluctuations in properties of gelatin. Processes of formation of gas bubbles were studied with changes in pressure both from high to normal (atmospheric) and from normal to low. It was found that with decompression to 60-80 mm Hg bubbles appear within a few seconds and grow intensively for 30-60 s. At 18°C temperature in 50-ml specimens with a gelatin concentration of 1.5 and 2.5%, their number constitutes 170 ± 50 and 940 ± 360 , respectively. When the temperature is lowered to 3°C, the number of bubbles in these samples decreases to 110 ± 20 and 440 ± 170 . With decompression from high to normal pressure, the bubbles grow for 30-40 min. Decompression from higher pressure levels leads to increase in quantity of bubbles formed in gelatin. In addition to pressure changes, the number of bubbles also depends on concentration of gelatin: an increase in the latter, other conditions being equal, elicits an increase in number of bubbles.

It is believed that, during decompression, bubbles are formed from nuclei, which already exist in the specimen at the time of decompression. Evidently, nuclei are formed in gelatin as a result of local tension of molecules that occurs when gelatin is submitted to thermal and mechanical treatment in the course of preparing the specimen, while part of the nuclei originate exogenously, entering with microscopic solid particles in water and gelatin, as indicated by the fact that the quantity of bubbles depends on the concentration of gelatin.

These studies revealed that bubble nuclei can persist in media for a long time. A model was proposed to explain the possibility of long-term existence of nuclei, which takes into consideration, in addition to force of surface tension, the elastic force generated by solid hydrophobic particles to which the nuclei are attached, or protein sheaths around nuclei that do not obstruct diffusion exchange of gases between the nucleus and medium around it.

4 illustrations, 9 references.

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